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AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

THE PLENTIFUL RARE EARTHS

some facts about a clubby clan of elements that are rare in name only

a report by LINDSAY

We got to thinking the other day that perhaps a lot of industry folks are passing up a diamond-studded opportunity because they believe the rare earths are unavailable in commercial tonnages. Nothing could be farther from the truth. Rare earths are *not* rare! Commercial salts of the rare earths are available, right now, for prompt shipment in quantities from a gram to a carload.

That the rare earths are so plentiful is due, in large part, to Lindsay. During the last 50 years, Lindsay has developed the extraction and separation of rare earths to a high degree.

New equipment and processes are now in operation at Lindsay's West Chicago plant and are producing greater quantities of these versatile materials in higher purities than before.

FROM 57 THROUGH 71—Some chemists call rare earths Lanthanides, Lanthanons or the Lanthanum Series. Actually they are not earths, but trivalent metals, a rather amazing family of elements . . . atomic numbers 57 through 71. They are grouped together because they are always found together, with thorium and yttrium, in ores such as monazite, and all have closely related properties. While rare earths are technically metals, Lindsay produces them in chemical salt forms—individually or in combinations.

ATOMIC NUMBER	ELEMENT
39	Yttrium
57	Lanthanum
58	Cerium
59	Praseodymium
60	Neodymium
62	Samarium
63	Europium
64	Gadolinium
65	Terbium
66	Dysprosium
67	Holmium
68	Erbium
69	Thulium
70	Ytterbium
71	Lutetium
90	Thorium

SOME USES FOR RARE EARTHS

LANTHANUM—As lanthanum oxide in a high refractive optical glass, particularly for aerial cameras and other instruments.

CERIUM—Glass polishing. Scavenger in explosives production. Radiation protection glass for atomic reactors. Opacifier for porcelain. Oxidizing catalysts in organic preparations. Ultraviolet light absorber.

MIXED RARE EARTHS—Misch metal for lighter flints and alloy uses. Motion sickness medication. Cores of arc carbon electrodes. Aluminum and magnesium alloys.

PRASEODYMIUM & NEODYMIUM—Dichroic colorants for ceramic glazes and glass. Used in better grade sun glasses. They do not lower light permeability and index of refraction when used as colorant or decolorizer. Ceramic capacitors.

The rare earths are becoming increasingly important in the production of steel and steel alloys. Small quantities added to the metal in the ladle result in a strong, fine-grained steel. Steel thus treated has great resistance to low temperature oxidation and corrosion. Stainless varieties have better hot and cold workability. Silicon and electrical grade steels have better electrical qualities.

Rare earths added to cast iron act as powerful deoxidizers and help remove sulfur from the molten metal. They are responsible for cast iron that is resistant to scaling at higher temperatures and to certain corrosive atmospheres. In malleable metals, they act as a carbide stabilizer.

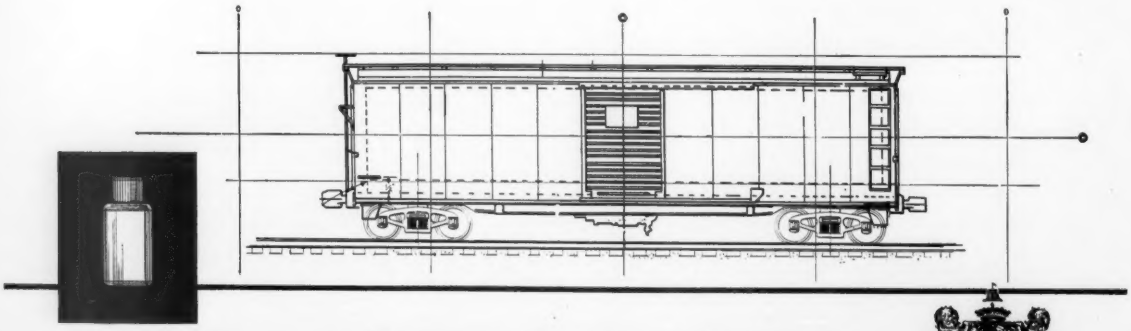
Magnesium-rare earth-zirconium alloys have excellent casting qualities and mechanical properties that make them ideal for important light-weight stressed components of aircraft engines.

Other rare earth compounds are used extensively for waterproofing, mildewproofing, weighting and dyeing of fabrics and compounding printing inks and phosphors.

LIKE AN ICEBERG—You might compare uses for the rare earths to an iceberg. What you see is only a small part of what lies undiscovered under the surface. In all probability, there is a real place for one or more of the rare earths in your operations. New uses—and profitable ones, too—are being discovered constantly. These versatile elements offer so much promise in so many different ways they merit your investigation.

To industries interested in the rare earths, we offer detailed technological data compiled over the years by our research staff. We will also furnish samples for experimentation.

And please remember . . . the rare earths are *plentiful*. Lindsay can supply you with quantities from a gram to a carload.



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SCIENCE

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Sources of Research Support

"Can you please tell me where I can get a grant for a research project on . . . ?" In one form or another this request comes fairly frequently to the AAAS office, as it does to the offices of other scientific associations and agencies. We should like to help the authors of these requests, but our judgment of the merits of a proposal is not really relevant, and our advice on possible sources of support is likely to be poorer, and certain to be slower, than information the authors can get for themselves from easily available sources.

These requests seem to indicate a failure of communication. The prospective grantee may not know it, but he has access to considerably fuller information than we or any other remote adviser can give him. As a start, he can consult *America's Foundations and Their Fields* [American Foundation Information Service, 860 Broadway, New York]. This useful volume describes the objectives and programs of 4162 foundations, indicates the fields supported by each, and contains an index of fields that will help anyone to select the foundations that *might* be interested in his particular proposal. A prospective grantee will find it both useful and interesting to spend a couple of hours studying this reference source.

The American Foundation Information Service also publishes *American Foundation News,* a periodical report of foundation grants and policies.

More detailed information can be found in the reports—usually published annually—that most of the major foundations distribute widely to university and large public libraries. These reports list the grants that a foundation has made during the preceding year, name the recipient of each, give a brief description or the title of the project or study, and usually state the amount of money granted. The National Science Foundation publishes a similar report, and comparable information is available from some of the other research-supporting agencies of the Federal Government. A list of studies currently being supported by a foundation can give a prospective grantee a fairly clear idea of whether or not that foundation is likely to give consideration to his proposal. If a foundation changes or extends its area of activity, an announcement of the change can be expected in its annual report.

Foundation officials are always searching for good studies to support. Only through their wisdom, imagination, and hard work has the business of giving money away become the successful and constructive affair that it is. Through their published reports they do their share and perhaps more than their share of trying to communicate with prospective grantees. As a further aid to good communication, the Carnegie Corporation has underwritten the recently established Foundation Library Center at 588 Fifth Avenue, New York. While the center cannot tell those in search of funds where to apply, it will become a major new source of information about foundations and their activities. The center plans to publish periodically a directory of foundation information.

If a prospective grantee does not know about the sources of information, perhaps this editorial will be helpful. If he does know of the available sources, he should use them. Better than anyone else, he knows what he wants to do; with the information about foundations that is available to him, he and his research colleagues are likely to be their own best advisers about appropriate sources of support.—D. W.

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Mode of Action of Penicillin

Biochemical Basis for the Mechanism of Action of Penicillin and for Its Selective Toxicity

James T. Park and Jack L. Strominger

In 1949, Park and Johnson (*1*) reported that uridine nucleotides accumulated in a *Staphylococcus aureus* that was inhibited by penicillin. Later, three previously unknown uridine nucleotides were separated and identified (*2*). The principal compound was uridine-5′-pyrophosphate linked to an unidentified N-acetyl-amino sugar and a peptide composed of D-glutamic acid, L-lysine, and DL-alanine in the ratio of 1/1/3 (Fig. 1). Several features of the accumulation of these nucleotides—the time sequence of accumulation after addition of penicillin, the relationship of accumulation to the threshold bacteriostatic concentration of penicillin, and the conditions under which accumulation could be demonstrated—have suggested that this phenomenon was a very early and specific effect of penicillin and might be closely related to the point of attack of penicillin within the bacterial cell (*2–4*). Uridine nucleotide accumulation was also found in a penicillin-sensitive *Lactobacillus helveticus* (*4, 5*) and similar compounds have been isolated from β-hemolytic streptococci (*6*).

The rate of accumulation of the peptide-containing uridine nucleotide in the presence of penicillin indicated that, if it were metabolized at this rate under normal conditions, it must be used in one of the principal synthetic reactions of the cell (*2–4*). At that time, the new amino sugar and D-amino acids were not known to be important in bacterial metabolism, and the product of the hypothetical reaction remained obscure. However, we now wish to present evidence that a structure analogous to part of the nucleotide is found in the cell wall of *Staphyoloccus aureus* and that the compound is presumably a biosynthetic precursor of the bacterial cell wall (*7*).

Dr. Park is a staff member of the Germ-free Animal Research Unit of the University of Pennsylvania, which is located at the Walter Reed Army Institute of Research, Washington, D.C. Dr. Strominger is a staff member of the department of pharmacology, Washington University School of Medicine, St. Louis, Mo.

Nature of the Cell Wall

In the past few years, a considerable amount of information concerning the nature of the bacterial cell wall has been obtained. Weibull (*8*) showed that, when a susceptible microorganism was treated with lysozyme in 0.2*M* sucrose, the lytic reaction was limited to removal of the external coat of the bacteria. The resulting spherical body, the protoplast, was composed of the bacterial cytoplasm with its limiting membrane (*9*). These observations clearly defined the cell wall as the rigid structure that gives shape to the bacterium and serves to protect the fragile protoplast. Cytological observations have also clearly differentiated the cell wall from the cell membrane (*10*), as well as from the extracellular capsule that is possessed by some microorganisms, and have indicated that growth of the cell wall during multiplication is always external to the cytoplasmic membrane (*11*).

Following the development of methods for preparing bacterial cell walls, a number of reports of their composition appeared (*12, 13*). Alanine, glutamic acid, and lysine (or, in some bacteria, diaminopimelic acid instead of lysine) are present in high concentration in the walls of all the gram-positive organisms that have been examined. Usually these are the only amino acids found in high concentration, although staphylococcal walls also contain glycine and the walls of some lactobacilli contain aspartic acid in high concentration (*13*). Recently, Snell and his coworkers (*14*) have reported that a large percentage of the alanine and glutamic acid in the cell walls of *Lactobacillus casei* and *Streptococcus faecalis* is in the D-form. These results suggest that DL-alanine, D-glutamic acid, and lysine (or diaminopimelic acid) are constituents of many bacterial cell walls.

Another line of investigation pertinent to understanding of the structure of the cell wall began with the observation of Strange and Powell (*15*) that a peptide derived from the spores of gram-positive bacilli was composed of alanine, glutamic acid, diaminopimelic acid, and an unidentified amino sugar. Cummins and Harris (*13*) have found this new amino sugar in the cell wall of a large variety of gram-positive bacteria, in more than 60 strains in all. The sugar was crystallized by Strange and Dark (*16*), and recently Strange (*17*) has proposed that its structure is 3-O-carboxyethyl hexosamine (see Fig. 1).

These analytic data strongly suggested a close similarity between the structures of a part of the cell wall and of a part of the uridine nucleotide that accumulates in penicillin-treated *Staphylococcus aureus*. Careful quantitative analyses of the cell walls of *S. aureus* were therefore carried out (*18*). The results are summarized in Table 1. The ratio of the new amino sugar, glutamic acid, lysine, and alanine in the cell wall approached 1/1/1/3, the ratio found in the nucleotide. Analysis of the optical rotation of the isolated alanine and glutamic acid by means of enzymes specific for D- or L-amino acids indicated that 45 percent of the alanine and 92 percent of the glutamic acid was in the D-form, compared with previously reported values of 52 percent and 100 percent for these amino acids in the nucleotide (*2*).

The unique amino sugar of the cell wall was identical with the amino sugar from the nucleotide, as is indicated by the following criteria which clearly distinguish it from glucosamine, galactosamine, or aminoglucuronic acid (*19*): (i) paper chromatography in three solvents; (ii) paper electrophoresis at several *p*H values from 2 to 6 (these data indicated that the compound contains a dissociable acid group with a *pK* around 2.5); (iii)

behavior of the N-acetylated amino sugar in a modified Morgan and Elson reaction (*20*) in different buffers; (iv) orange-pink color formed in a modified Elson and Morgan reaction (*21*) with maximum absorption at 506 millimicrons; (v) paper chromatography of the ninhydrin degradation product (*22*); and (vi) behavior in cation-exchange chromatography.

Furthermore, limited acid hydrolysis of the cell wall has yielded fragments that are very similar to fragments derived by similar treatment of the nucleotide (*23*). Exact comparison depends on further identification of these fragments. It may be emphasized that two of the compounds, D-alanine and 3-O-carboxyethyl hexosamine, have not been found elsewhere in nature and that D-glutamic acid is an unusual natural substance.

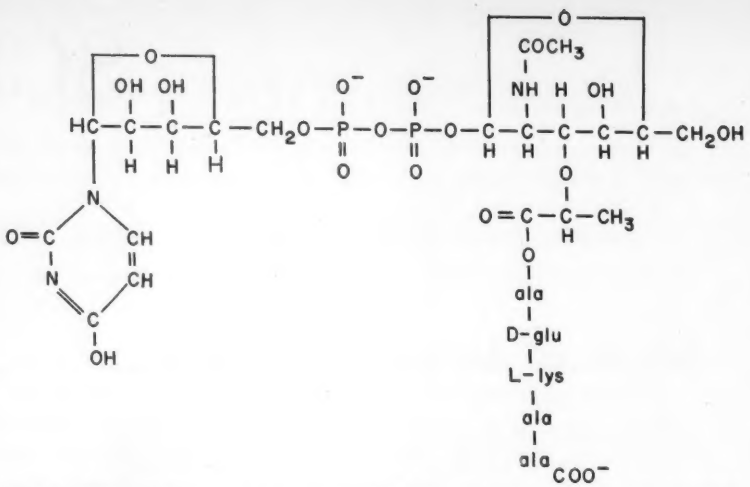

Fig. 1. Proposed structure of the principal nucleotide that accumulates in penicillin-treated *Staphylococcus aureus*. In addition to the original structural determination of Park (*2*), this structure incorporates a structure proposed for the amino sugar by Strange (*17*). The sequence of amino acids in the peptide is one of the possible sequences indicated by Strominger (*5, 32*).

Mechanism of Action

The uniqueness of the structures in the wall and in the nucleotide suggests that they may be metabolically related. Moreover, the striking similarity of structure, as well as the biological experiments, leads to the conclusion that the uridine pyrophosphate N-acetylamino sugar peptide is a biosynthetic precursor of the bacterial cell wall, and that the accumulation of this compound in penicillin-treated *Staphylococcus aureus* is the consequence of the interference by penicillin with the biosynthesis of the cell wall. Uridine pyrophosphate glycosyl compounds are activated intermediates in many biosynthetic transglycosidation reactions, and the N-acetylamino sugar peptide may be considered as a nucleotidyl fragment activated for such a synthetic reaction. The transfer of this fragment from the nucleotide to some cell wall acceptor would be a reaction for which many models now exist (*24*).

The exact nature of the interference by penicillin is a matter of speculation. It seems possible that penicillin is a specific inhibitor of the transglycosidation reaction involving this uridine nucleotide.

Data on the binding of penicillin by bacteria are consistent with this formulation. Maas and Johnson (*25*) and Cooper and Rowley (*26*) independently demonstrated that staphylococci specifically and firmly bound about 1000 molecules of penicillin per cell (possibly a titration of the number of molecules of a specific enzyme). Cooper (*27*) has shown that the penicillin is bound to a lipid-containing fraction close to the cell wall. The binding by these lipid particles was 7 to 12 times that of whole cells on a weight basis.

From the recent report of Mitchell and Moyle (*28*) it seems clear that the particles which bind penicillin were originally cell membrane. Thus the hypothetical transglycosidase, were it also the specific binding site of penicillin, is strategically located to transfer the N-acetylamino sugar peptide from uridine pyrophosphate, which is inside the membrane, to an acceptor (cell-wall site) outside the membrane. Indeed, the cell membrane may well be the location of many transglycosidases that appear to participate in synthesis of extracellular polysaccharides from intracellular uridine pyrophosphate glycosyl compounds.

It has been calculated (*3*) that if penicillin-binding inhibits the enzyme that normally utilizes the uridine pyrophosphate derivatives, this enzyme would have a turnover number of about 6000. It can now be calculated that a staphylococcus with a generation time of 1 hour and 1 percent of whose weight is 3-O-carboxyethyl hexosamine (the situation with strain 2) would require 1000 molecules of enzyme with a turnover number of about 6000 to incorporate the N-acetylamino sugar peptide into the wall at the observed rate. Therefore, on a kinetic basis, the rate of synthesis of uridine pyrophosphate derivatives is comparable to the rate at which they would normally be utilized if the N-acetylamino sugar peptide is incorporated into the cell wall. It must be pointed out that, until a membrane fragment is obtained which will catalyze the proposed transglycosidase reaction and until it is shown that this reaction is sensitive to penicillin, interference with cell-wall synthesis by blockage of a single reaction is not proved. More complicated mechanisms for transfer of the N-acetylamino sugar peptide through the membrane and into the cell wall can also be visualized. For example, accumulation of the nucleotide might occur if penicillin blocked the synthesis of the acceptor site in the cell wall.

Table 1. Comparison of analysis of the cell wall and of a uridine nucleotide that accumulates in penicillin-treated *Staphylococcus aureus*. Data are given as the ratio to the amount of glutamic acid. The cell walls were prepared by the method of Salton and Horne (*33*). After acid hydrolysis, the products were separated on Dowex-50. The only other ninhydrin-positive components present were glucosamine (ratio about 2 when corrected for loss due to acid hydrolysis), glycine (ratio 3.8), NH_3 and, in the case of strain 1, a small amount of an unidentified substance (*18*).

Compound	Cell walls		Uridine nucleotide
	Strain 1	Strain 2	
Glutamic acid	(1)	(1)	1
Lysine	0.95	1.17	1.0
Alanine	3.2	3.5	3.0
3-O-Carboxyethyl hexosamine	0.23*	0.93	1.0

* The low value for the new amino sugar in this case was owing to destruction as a result of prolonged acid hydrolysis (6*N* HCl at 100°C for 15 hours). When this value was corrected by the amount of ammonia present, a value close to 1 was obtained (*18*).

Selective Toxicity

The familiar effects of penicillin on morphology of bacteria—swelling, filamentous forms, large body formation, production of the penicillin-insensitive

L-forms of bacteria, and lysis—are all explained by the loss of the integrity of the cell wall that follows interruption of cell-wall synthesis. Simultaneously with our work, Lederberg has shown that *Escherichia coli* cells are quantitatively converted to protoplasts in the presence of penicillin and sucrose. The protoplasts reverted to bacilli after removal of penicillin, thus showing that the cells retained their full capacities. We believe that Lederberg has correctly interpreted these morphological observations as evidence that penicillin interferes with maintenance of the cell wall or with its synthesis (*29*). Hahn and Ciak have studied lysis of *E. coli* in the presence of penicillin and have also postulated that loss of cell-wall integrity induced by the drug is responsible (*30*).

In our view, therefore, the selective toxicity of penicillin is due to its interference in a metabolic sequence that is not found in animal cells, the biosynthesis of the cell wall. Crystal violet, another antibacterial substance also bound in the cell membrane or wall, seems to inhibit the same metabolic sequence, although at a different point (*31*). Possibly other antibacterial substances may owe their selective toxicity to interference at some point in this reaction sequence.

It seems attractive to speculate further that competitive inhibitors related to the several unique components of the wall and nucleotide, and which would be useful as chemotherapeutic agents, might now be devised. Purification and study of the reactions leading to synthesis of the wall might also contribute greatly to this goal, and the availability of uridine nucleotide intermediates suggests that this possibility lies in the not-too-distant future.

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Scientific Communications Should Be Improved

Fred W. Decker

Authentic, complete, prompt, and understandable reports of scientific developments have always been needed, and in the past they have always inestimably aided scientific achievement. The accelerated pace of science today requires more than ever the aid of full and accurate communications among science, business, and the public. However, during the past decade some questions of ethics and communications have grown until they now threaten to hamper critically the status of science in modern society. These questions demand review and action by the scientific community at large. The time is long overdue for all scientists to examine these questions in the contexts of their own professional fields and to share with other scientists their experiences in improving scientific communications.

Channels

Information about developments on the scientific frontier may reach the public through the channels of professional publications, newspapers, or advertising. All channels of communication are active when technologic development has economic implications. "Scientific facts" may then be proclaimed by several parties, and the public is thoroughly confused by sharply conflicting "scientific" conclusions.

Science is represented to society not only by qualified impartial scientists guided by objective logic but also by specialists and former scientists whose scientific conscience may have been more or less eroded by commercial interests, by specialists not broadly enough trained to speak with adequate perspective, by promoters operating on the fringe of science with little or no concern for the long-range growth of science, and by outright charlatans totally unqualified in science but yet accepted by many laymen as "scientists." Moreover, journalistic practices tend to aid the spectacular claims more than the cautious, qualified reports. Demands for brevity sometimes cause omission of essential features even in valid statements and leave erroneous impressions.

Several recent cases demonstrate a need for researchers to give special attention to examining their means of communication with one another and with the public on the results of scientific investigations. Conflicting reports have appeared, and in some cases controversy has raged over such subjects as battery

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additives, lung cancer, fluoridation, cloud seeding, the Salk vaccine, and radiation danger. Press reports to the public have featured assertions and counterassertions. Research scientists cannot ignore the means for dissemination of their research results. Today, the financial support of research is being generously provided by members and leaders of society who cannot reasonably be expected to search the technical journals to learn what science is accomplishing. To gain public attention for candid, understandable, and prompt reports on advances in science and to avoid the diversion of public support to pseudo science are among the problems the scientific community must face.

Consider, for instance, the controversial field of cloud seeding. In the past decade the effort to modify the weather has grown from the research stage into a full-blown, million-dollar industry with a dozen companies active in the United States (*1*). At the same time, a sharp controversy has developed over the basis for evaluating and accepting the claims of the commercial operators. Thus, within the past few years we have seen the growth of an industry representing itself as "scientific" while many impartial scientists are extremely skeptical of the broad claims advanced or implied by promoters of that industry. Compressed within a short life-span, the field of cloud seeding presents an excellent case study involving a number of questions of scientific ethics, policy, and communications which can arise and have arisen in other fields of scientific endeavor.

In listing a number of these questions in subsequent sections, I have cited illustrations drawn from the controversial field of cloud seeding, because in this field I have repeatedly come face to face with many of the potential weaknesses in the existing communications between scientists and the general public. Other scientists may recognize counterparts to these illustrations in their own fields. If so, the scientists confronting these specific issues will gratefully receive the suggestions of fellow-scientists about the best means for handling them. Since others may be confronted by different problems in the general area of communications and policy, it is to be hoped that the channels of scientific publication will remain open to the free expression of the issues and the discussion of solutions to the pressing problems in the relationships between science and society.

Evidence

What constitutes "scientific evidence?" What shall scientists, by precept and example, use as evidence in arriving at conclusions? Dismayed scientists recently learned that the testimonials of 45 satisfied users of a battery additive could help to offset research by the National Bureau of Standards in the deliberations of the Federal Trade Commission. Similarly, testimony by 92 satisfied users of a colorfully advertised water conditioner outweighed the opinions and tests of 22 scientists (*2*).

Validity of data should be a primary concern of everyone in this scientific age. Has the impact of science on society failed to produce a realization that unqualified testimonials have no standing against objective tests? Has the "anything goes" practice of some advertisers gained ascendancy even in this "scientific age?" For example, commercial cloud seeders have urged independent evaluators to base their conclusions at least partially on "going out and *seeing* the operations," but many evaluators have been reluctant to accept "data" that are not based on actual measurement, perhaps taking their cue from Kelvin. Unless scientists insist on a standard of objectivity for data, the term *scientifically proved* (or disproved) can easily fall into public disrepute. To prevent this, science must somehow overcome certain commercial interests and enlist the aid of a press that sometimes is either indifferent or hostile.

Experimentation

What constitutes "scientific experimentation?" Well-designed experiments do not happen spontaneously but are the results of careful planning and consultation. However, so-called "experiments" are often conducted for the purpose of obtaining visual or numerical comparisons where such comparisons may not be valid because extraneous factors were not removed from the operations leading to the comparisons. Moreover, the experiment sometimes is valid enough but does not actually deal with the announced subject.

For example, experiments in cold boxes and in the free atmosphere to alter clouds with Dry Ice or silver iodide are often mentioned in publicity about cloud seeding to increase rainfall. However, those cloud-modification experiments did not necessarily concern increased rainfall, and adequate measurements were not made which would permit testing for increased rainfall.

Proof

How much proof must be offered to support conclusions? Scientists agree that conclusions must be based on a careful analysis of all the pertinent data. There can be no suppression of inconvenient data that contribute to statistical variation and tend to undermine or blur the conclusion. Conclusions can be drawn most readily when observed measurements are closely correlated with the variable factors. In the cloud-seeding case, unfortunately, wide variations appear between natural rainfall and computed amounts, even when elaborate multiple-regression equations employing numerous factors related to the amount of precipitation are used (*3*). Then the question arises about how far the actual precipitation must depart from the computed amount to justify labeling it the work of cloud seeding, not merely natural, chance variation.

Disregarding for the moment the considerations of economic speculation, what degree of doubt will scientists accept while being satisfied with a conclusion? This question is complicated by the fact that setting up too stringent a requirement for proof could cause rejection of a valid claim, while relaxing the requirements could produce acceptance of false claims. Because of the inherent uncertainties of historical comparisons and because of the meager data available for evaluation of cloud seeding, one evaluation group compromised between these two kinds of error by adopting a standard of acceptance so low that there was admittedly appreciable danger of declaring that cloud seeding had increased the rainfall even it it had actually decreased the rainfall. Evidently the solution is to use designed experiments that minimize the sources of this error (*4*). The widely advertised commercial rain-making operations have not provided data genuinely satisfactory for evaluation, a point on which agreement was apparent in reports of the Conference on the Scientific Basis of Weather Modification Studies at Tucson, Arizona, 10–12 April 1956 (*5*).

Publication

What scientific work must be published by ethical researchers? The whole structure of science is based on the free exchange of information and not on the hermitlike total security of the alchemist. Research scientists owe other workers in the field publication complete enough to add to the scientific capital with which all must work. Entrepreneurs who want to retain trade secrets should not give the impression that they are speaking as scientists if they announce results without giving the substantial basis for their conclusions.

The claims advanced by some meteorologists in the cloud-seeding business, for instance, create the impression that scientists habitually announce results without subjecting their conclusions to the scrutiny of the rest of the scientific world. With few exceptions, the commercial cloud seeders have failed to pub-

lish their work in the scientific journals (*6*). Even an evaluating federal agency, after announcing conclusions favorable to some of the rain makers' claims in February 1956, has failed to publish any technical report to explain those conclusions.

Researchers should expect to be judged by the promptness and completeness of their reporting. Could not scientific societies prepare and publicize candid descriptions of promotional statements circulated under the label of science, categorizing them when appropriate as "never submitted for review by scientists in this field," "generally regarded as unsupported by the scientists in this field," "subject of debate and probably a moot question," and so forth? Should not scientists in public positions expect to give the technical basis when they are announcing their conclusions rather than to allow lengthy delays between the announcement of conclusions and the release of technical reports? Cannot scientists and editors generally encourage professional publication in order to offset the tendency toward publicizing unsubstantiated claims and insist that such reports reveal the evidence supporting the claims and conclusions?

Public Release of Technical Details

How should technical details of scientific research be described in popular releases? Understandable reports by research scientists are particularly hard for the public to obtain (*7*). Not only are scientists sometimes inarticulate even to specialists in nearby fields, but the Fourth Estate finds it particularly hard to secure usable information. The terminology sometimes employed by scientists is obscure or actually misleading. "Statistically significant," for instance, to a layman probably means "large," whereas to the specialist it may mean "large enough (by some required departure) to abandon the null hypothesis."

Science will not profit by permitting nomenclature to develop without regard to the impressions created. For example, in the use of the term *statistically significant,* some cloud-seeding evaluators have omitted to specify the standard of rarity required for "significance." Thus, one agency that was using an unannounced low standard of acceptance declared that cloud seeding "significantly" increased rain on the same project in which another agency that was using a more severe standard of acceptance found no significant increase in rainfall. Certainly all pertinent details must be revealed if such reports are not to appear contradictory.

Scientists can make a real contribution to the general public understanding of science by adopting more specific and understandable language. The language used should be understandable at least to the elements of society concerned with making decisions on the basis of such reports. In this matter, we again see illustrated the need for continuing education in science starting in school and continuing through the functioning of communications aimed at keeping the public abreast of the times. In view of the role of science in modern life, can we be satisfied with the amount of attention directed to understanding the trends and events in science on the part of the lay public?

Margin of Uncertainty

How should scientists describe the nature of their discoveries? Scientific progress has come from the pains-taking solution of the small problems that are parts of the larger problems. Newton recognized that his accomplishments came from "standing on the shoulders of giants." Such expressions of humility might be overlooked in the headlong rush of science toward the discoveries of the past 25 years, but can scientists really afford some of the publicity about their work? *Scientific breakthrough* is a phrase increasingly used in science news stories. Scientists will do well to remind all concerned that in their conclusions there is always a margin of uncertainty.

Fortunately, the science of statistics furnishes excellent means for defining the area of uncertainty. That the public does not always hear of this uncertainty is illustrated by the repeated claims by commercial cloud seeders pointing to extraordinary increases in precipitation. Sometimes not even a day elapses between the rainfall and the confident announcement that cloud seeding produced more rain than would have fallen naturally (*8*). Drouth-breaking rains have been claimed by the rain makers, even though the available measurements are too meager to support the claims with any appreciable confidence. Some segments of the public seem already to have associated the term *rain maker* with exaggeration and overzealous salesmanship involving a dubious product, as witness the use of the term to describe Soviet diplomats visiting India (*9*).

Overstatement of Results

Will overstatement of results choke off future development? When research seems to have succeeded, the drive for new discoveries may slacken. Having achieved the goal, scientists may look toward new challenging areas, and financial support quite logically shifts. Referring again to cloud seeding, large sums of money are being spent for operations that are based on the assumption that various processes are actually producing economically important changes in the precipitation pattern. Cloud-seeding operations that were initiated as "applied research" are usually proceeding now without any effective evaluation checks. Operations are conducted dogmatically, despite the inability of statistical analysis to attribute favorable results to cloud seeding with any high level of confidence.

Actually, the technical basis for cloud seeding is not at all settled. It seems highly probable that important discoveries remain to be made in this field. The physical and chemical nature of effective seeding agents must be established definitely. It is not even certain that flame-type silver iodide generators are producing silver iodide crystals. Moreover, the atmospheric mixing processes should be investigated; there is some question whether the seeding agents are really carried rapidly enough above the freezing level (*10*). These uncertainties must be faced frankly, not submerged by glittering claims of success, if progress is to be made. There would appear to be a point of broad scientific importance in this aspect of cloud-seeding work and publicity.

Exploitation prior to Verification

Can an unsettled technical process be exploited commercially prior to full verification? When this type of problem arose during World War II, "field service tests" were conducted where the equipment might contribute a critical advantage, even though the equipment was still undergoing development. Clients who were unwilling to forego hail-suppression activities for the periods needed to establish "nonseeded" storm records for comparisons could now set up "hail-suppression proving grounds." There the various claims could be examined, and possibly the processes could be developed and optimized while the field operations continued on the clients' target areas. It could even be argued that the doctrine of *caveat emptor* obliges the client to be wary and to adopt measures calculated to protect his own interests.

The scientist is, in such cases, under obligation to lend his support and assistance to submit to impartial tests the claims for new techniques whenever the name of science is used directly or indirectly to sell the innovation to the public. Failure to do this can only prejudice the position of science in our society.

Unfortunately, when designed experiments are proposed aiming at creating the necessary observational network and working toward optimizing the process of cloud seeding, certain commercial

cloud-seeding meteorologists stoutly and openly oppose such experiments. Is not the individual's scientific stature directly related to the alacrity with which he adopts such objective experimental methods? Perhaps the controlled experiment starting in 1957 at Santa Barbara, California, will establish a new pattern for other commercial rain-making attempts.

Bases of Decisions

Can scientists assist in making decisions when "scientific proof" seems to be lacking? An objective criterion is needed for deciding whether to continue a service like cloud seeding in the absence of acceptable scientific proof that the claims of success are valid. Clients are told that they cannot afford to omit the service because the cost is small compared with the claimed benefits. However, to accept all such proposals can bankrupt the client.

Scientists who are attempting to determine for the client whether the process is an acceptable business gamble would do well to avoid such expressions as *statistically significant* and, instead, to use language that clearly distinguishes the results as an estimate of business risk which does not imply proof.

Acceptance of Authentic Work

What must scientists do to assure acceptance of their work as authentic? Cultivation of ethical practices in science will earn public recognition and confidence in scientific results. The increasingly intimate relationship of many branches of science to society calls for the kind of review that produced the Hippocratic Oath in medicine. Clearly defined duties of the scientist to society can avert misunderstandings and increase society's recognition of science. Laymen who turn to scientists for expert advice on goods and services should have no doubts concerning the scientists' independence of judgment.

Even valid findings can be suspect if the scientists or individuals who are retained as scientists by the buyer should soon enter the services of the seller. Individuals who are accepted as scientists by the public can bring discredit upon the scientific community by such action, even when their individual motives are quite innocent. Can scientists find a way to avoid the misunderstandings that develop when, for instance, either scientific or executive personnel of an evaluation agency leave to engage in commercial rain making after the agency has published a controversial endorsement of cloud seeders' claims?

Open Criticism

Can science afford an absence of open criticism? Contemporary writers have observed a decline of criticism in literature, and a similar euphemistic tendency may well be developing in science. For instance, critics who point to the uncertainties in the cloud-seeding claims are now falsely labeled as "negativists" or "obstructionists" and are accused of assuming a "can't do" attitude. The critics' valuable role in the advance of science could be stifled if the scientific world does not rally to insist on recognition for those who call for scientific proof, not advertising claims. Being human, they must eventually bow, as did Galileo, if other scientists will not stand with them.

In this regard, every scientist should carry the message that there are in reality the following three categories of individuals in any scientific controversy over conclusions: (i) the enthusiastic innovators; (ii) those who conclude that the innovators are wrong; and (iii) those who insist on obtaining more definitive data before they join either of the first two groups. A scientific tragedy today is that often the third group is ignored and carelessly classed with the second group.

Science cannot progress without searching inquiries developed by those who reserve judgment and will not hastily accept conclusions or dogma. Hoaxes like the "Piltdown man" (*11*) should stand as warnings to any who would cry down the independent critics. Teachers of science should contribute to public appreciation of scientific critics by emphasizing with Conant that "the innovator is by no means always right" and should prove this to their students with cases "where some bold man put forth a new idea based on alleged facts that turned out to be erroneous or erroneously interpreted" (*12*).

Public Understanding and Appreciation

How can science gain better understanding and appreciation from the public? This thorny problem has been faced, for instance, by the medical profession for many years. People often are willing to believe that a profession or an industry has conspired to suppress truth or new discoveries. Such canards easily gain attention, but their refutation gets little attention or acceptance. Playing upon the desires and suspicions of the people and making a great show of zealous effort, clever promoters today demonstrate the truth of Caesar's observation that "in most cases men willingly believe what they wish" (*13*).

For instance, in contract negotiations many of the rain makers stress the need of the client for water, the earnestness of the seeder, the size and versatility of the seeding organization, and the fringe services to be rendered. However, they have generally omitted the specific engineering details of the "experiments" to be conducted and have neglected to supply the valid technical reports that might be expected from experiments. A few of them have diverted attention by attacking valid scientific research which is in progress.

Confronted by the inability of many of the public to understand scientific method, results, and language, scientists could easily abandon any hope of a *rapprochement* with society. The methods and facts of science have advanced so far as to leave some of the most learned and influential professions "behind the pace of the times" (*14*). This situation is not the fault of the scientists, but perhaps only they can solve it. A well-organized, continuing effort by the scientific community as a whole could produce a keener understanding of science, particularly if this effort included "progress reports" in science and if it reached teachers, students, and the public generally.

Ultimately, the best hope is in developing a realization that, no matter how great the earnestness, hope, sincerity, or need of the would-be innovator, discoveries can occur only if they already exist in nature. All people should understand this fundamental if they are not to be disappointed and bilked and in order that they will continuously support the methodical work aimed at satisfying human needs and desires.

Conclusions

The world of science needs more than ever an active conscience in ethical dealings with the public, a clear understanding of the requirements of objectivity, the ability understandably to articulate the results of scientific work, and constructive criticism of both innovation and dogma.

Society today urgently needs a closer liaison leading to a more complete knowledge of the products of scientific work and a more general acceptance of the objective processes of scientific thought. Public leadership should foster a heightened appreciation of scientists and should not permit valid scientific work to be offset by promotionalism and unfounded charges. Scientists can inform, but other elements of society must seek knowledge and understanding of trends in science, if genuine progress in science is to be recognized and exploited. The public cannot hold the legitimate scientist to blame after the public has followed the promoter who scorns the disciplines of science. Keeping up with the pace of the times is still the duty of all.

Scientific societies should foster discussion of the means of scientific communication, develop clear codes of scientific ethics, and publicize information on the actual status of claims or discoveries, particularly when widespread publicity is being given to unproved or false claims.

Science should be interpreted to society generally through the use of "progress reports" on science which are aimed at demonstrating the methodical processes of research, the pitfalls and disappointments, and the philosophy of objective reasoning. Science news consists as much in the processes as in the final results. The effort required for such interpretation is not the obligation of scientists alone, but must be augmented by all the means described in the preceding paragraphs and by better interpretations in the mass media. It is an encouraging sign that science newswriters generally recognize these obligations and problems. Closer cooperation between scientists and science writers would result in a better general public understanding of science and scientific evidence.

Educators should explain the demands of scientific objectivity to their students. The mere teaching of subject content alone will not give assurance that the academically trained scientist is aware of the pitfalls of premature claims or the proper relations between science and society. Each future scientist should be taught the responsibilities of his position as a representative of science to society generally.

Every practicing scientist should reflect seriously on his own opportunities to assist in representing to the public the way in which science advances, the need for tests of the validity of conclusions, the logical processes of science, the demands for objectivity, the need for adequate and valid data, and the difference between claims and proved results. His own research reports should be models of objectivity and clarity. Performing this duty might not result in personal rewards, but scientists have a unique responsibility to see that false opinions do not eclipse the accurate information needed for progress.

Public confusion about the meaning of scientific work must eventually produce a negative reaction. Exaggeration and overselling in order to gain financial support for science will ultimately stand revealed. Unless such fringe practices have been publicly and specifically disowned by legitimate scientists, the reaction may affect all of science; then public confidence, understanding, and support may vanish. In that event, the scientific community may deeply regret having neglected to clarify the nature of science in the public mind. Scientific societies and individual scientists can lead to a solution by attracting more attention to the progress of science and by communicating with one another and with the rest of society in completely candid terms.

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Biochemical Mutations in Man and Microorganisms

Herman M. Kalckar

It is a well-known fact that normal development of mammals is possible without an external supply of galactose. Galactoside synthesis, especially of the complex galactosides that are constituents of cellular structures, is an essential feature of normal growth and development. Mammals, like most organisms, are able to convert glucose to galactosides. The galactolipids, for example, which constitute a large bulk of the brain, are examples of structural galactosides that are deposited exclusively after birth (*1*). As will be discussed in subsequent paragraphs, these compounds can be synthesized from dietary glucose as well as from dietary galactose.

The dispensability of galactose raises the question of why lactose is ubiquitous in mammalian species. It is possible that early in their evolution mammals were subjected to influences that made it advantageous for them to produce milk containing lactose for their progeny. The possible advantages of lactose in the diet of the progeny have not been explored. The influence of lactose on the bacterial flora of the gastrointestinal tract should certainly be considered, for the microorganisms in the intestine play a role in making certain vitamins available or unavailable to the host. It is known that replacement of lactose by sucrose in the diet greatly increases the need of the host organism for vitamins such as pyridoxine and riboflavin (*2*).

If galactose is administered externally, it is largely used as a fuel through conversion to glucose-6-phosphate. Most microorganisms use galactose for this purpose provided that they are able to adapt and that they cannot get access to glucose. Part of the administered galactose is used, as mentioned, for the synthesis of cellular galactosides.

Complexity of Galactose Metabolism

The activation of galactose, unlike that of glucose, is initiated through a direct phosphorylation of the reducing group, giving rise to α-galactose-1-phosphate (G-1-P) (Kosterlitz, *3*). The metabolic mobilization of galactose, also unlike that

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of glucose, requires an additional step beyond the phosphorylation step. The galactose-1-phosphate formed must be incorporated into a specific nucleotide of the type first discovered by Leloir and his coworkers (*4*). This is a peculiar "mongrel" of a dinucleotide in which 5-uridylic acid is linked to the phosphate of either α-glucose-1-phosphate [Cori ester (G-1-P)] or α-galactose-1-phosphate (Gal-1-P). This mongrel nucleotide is called uridine diphosphoglucose (UDPG) or uridine diphosphogalactose (UDPGal) (*5*).

The enzymatic interconversion of uridine diphosphoglucose and uridine diphosphogalactose was first described in crude extracts of galactose-adapted yeast (*6*). The enzyme was called "galacto-waldenase" in accordance with the term *galacto-walden inversion*, which had been used for a long time in reference to the interconversion of galactose to glucose.

At this point it is necessary to spend a few lines on terminology. The term *galacto-walden inversion* was never satisfactory because it implied that an "umbrella" type of inversion (first described by Walden) was operating on the rearrangement of the 4-hydroxyl group of galactose (or glucose), but this has never been proved to be the case. On the contrary, recent studies in our laboratory on highly fractionated galacto-waldenase from calf liver have shown an absolute requirement for a hydrogen-transferring system, namely diphosphopyridine nucleotide (*7*).

This observation points strongly in favor of an oxidation-reduction mechanism as the basis of the rearrangement (compare also *8*). We therefore propose the more correct and descriptive name, uridine diphosphogalactose 4-epimerase, for the enzyme that catalyzes the inversion, to replace the old name, galacto-waldenase (*9, 10*).

Congenital Galactosemia in Man

It is known that infants afflicted with the heritable human disease, congenital galactosemia, which deprives them of the ability to metabolize galactose, improve dramatically when they are put on a strict galactose-free diet (*11*). A lack of "galacto-waldenase" has often been cited as the probable biochemical lesion in galactosemia; especially after the observation was made that galactose-1-phosphate accumulates in the blood cells of galactosemic subjects (*12*). Such a biochemical lesion would, however, deprive the infants of the ability to make brain galactosides from glucose or other nutrients (*13*) and limit them to using administered galactose, which is known to be able to serve as a source of galactolipids (*14*). Whether an organism with such a deficiency and without any external supply of galactose would undergo normal growth and development is doubtful. An alternative would be deposition of glucolipids instead of galactolipids in brain. Would this be compatible with normal brain function?

It seems worth while to try to explore these problems in properly designed animal experiments. However, this aspect has become irrelevant in a discussion of the disease congenital galactosemia, for it has recently been shown that the enzyme block does not affect the uridine diphosphogalactose 4-epimerase proper (*15*) but affects another totally different type of enzyme. This is the enzyme that catalyzes the step prior to the inversion—that is, the incorporation of galactose-1-phosphate into uridine nucleotides according to the equation (*16, 17*)

$$\text{Gal-1-P} + \text{UDPG} \rightleftharpoons \text{G-1-P} + \text{UDPGal}$$

This enzyme, which "trades" the glucose-1-phosphate moiety of uridine diphosphoglucose for galactose-1-phosphate, can best be classified as a uridyl transferase (*18, 19*) in which galactose-1-phosphate or glucose-1-phosphate take their turn as nucleophilic agents for the uridyl fragment.

Another type of uridyl transferase affecting uridine diphosphoglucose, which was first described in yeast that was not adapted to galactose, catalyzes the following reaction (*18, 19*):

$$\text{UTP} + \text{G-1-P} \rightleftharpoons \text{UDPG} + \text{PP}$$

Here inorganic pyrophosphate (PP) takes the place of galactose-1-phosphate as the alternating nucleophilic reagent. The enzyme catalyzing this reaction belongs to the class that we have called pyrophosphate uridyl transferases because inorganic pyrophosphate is involved. Since there are other pyrophosphate uridyl transferases (*20*), it would be best to name the specific catalyst of the reaction "uridine diphosphoglucose pyrophosphorylase," in line with Kornberg's diphosphopyridine nucleotide pyrophosphorylase (*21*).

New Terminology

Let us summarize the pertinent points to recapitulate the new terminology.

1) Galactokinase catalyzes the phosphorylation of the reducing group of D-galactose (Gal.)

$$\text{Gal} + \text{ATP} \rightarrow \text{Gal-1-P} + \text{ADP} \quad (1)$$

2) Galactose-1-phosphate uridyl transferase catalyzes the incorporation of galactose-1-phosphate into a nucleotide.

$$\text{Gal-1-P} + \text{UDPG} \rightleftharpoons \text{G-1-P} + \text{UDPGal} \quad (2)$$

This is the catalyst that is defective in congenital human galactosemia.

3) Uridine diphosphogalactose 4-epimerase, having diphosphopyridine nucleotide as coenzyme, catalyzes the epimerization of the 4-hydroxyl group of the hexose moiety, presumably through an oxidation-reduction process in which a 4-keto sugar nucleotide (and reduced diphosphopyridine nucleotide) is a transitory product.

$$\text{UDPGal} \rightleftharpoons \text{UDPG} \quad (3)$$

4) Uridine diphosphoglucose pyrophosphorylase catalyzes the release of glucose-1-phosphate from uridine diphosphoglucose.

$$\text{UDPG} + \text{PP} \rightleftharpoons \text{UTP} + \text{G-1-P} \quad (4)$$

However, this can also be accomplished in reaction 2. More important, presumably, is the reaction from right to left in which uridine diphosphoglucose is synthesized from uridine triphosphate (UTP) and glucose-1-phosphate (*18*) or from uridine diphosphate, adenosine triphosphate (ATP), and glucose-1-phosphate (*22*). This is probably how the key substance, uridine diphosphoglucose, is initially formed in cellular metabolism.

Genes and Enzyme Synthesis

As mentioned here and in our earlier publications, the enzymes that catalyze steps 1, 3, and 4 are present in blood cells of galactosemic subjects as well as in normal cases. Only the enzyme catalyzing step 2 is defective. It should be emphasized that, although we have been able to demonstrate this major defect of galactose-1-phosphate uridyl transferase in more than 15 cases of this disease, it would be premature to classify even these cases as necessarily belonging to a biochemically homogenous disease. This is well illustrated in Kurahashi's article in this series (*23*). Kurahashi has found that among a number of galactose-negative mutants of *Escherichia coli*, K_{12} strain (*24*), four different mutants are lacking galactose-1-phosphate uridyl transferase. Although they all show the same biochemical defect, Morse, Lederberg, and Lederberg were able to show by means of their genetic techniques (*25*) that they are due to alterations in different, though closely located genes.

Yanowsky (*26*), working on *Neurospora*, was able to resolve the manifestations of such mutants by immunochemical techniques. In this work, instances are described in which the enzymatic activity was lost but in which the antigenic activity—that is, the ability to bind antienzymes—was preserved. Such a study is planned for the bacterial mutants in order to show the possible existence of

incomplete enzymes. This study may provide additional information about gene action and protein synthesis. It is sufficient at present to state that at least four genes are needed in *Escherichia coli* in order to insure a normal functioning galactose-1-phosphate uridyl transferase. Offhand, there is certainly no reason to believe that man should require fewer genes for the same purpose. Furthermore, there is no reason either to believe that the same gene is affected in different, unrelated families. Hence, there is obviously margin for biochemical variations if methods with finer resolutions are found.

The immunochemical approach seems particularly promising, but there are other possibilities that can most readily be tried on the bacterial mutants. If, for instance, one of the mutants lacks the ability to synthesize a cofactor but can synthesize the protein, the biochemical defect would look like a lack of galactose-1-phosphate uridyl transferase if the standard technique was used. However, if extracts of this mutant were combined with protein-free filtrate of a normal strain which would supply this cofactor, activity might be restored.

These considerations have direct bearings on the approach in a further study of human galactosemia. We had earlier tried such a type of extract-recombination experiment in two galactosemic families, but we found no reactivation (*17*). However, for the reasons just stated, such reactivation attempts should be applied for each galactosemic family studied, for each family would count as a different case despite the seemingly identical enzymatic defect.

Congenital Galactosemia, a General Tissue Defect

The importance of assaying more than one type of cell or tissue is evident from the article by Anderson *et al.* in this series (*27*). In one case, a 24-year old boy with diagnosed congenital galactosemia showed a small but definite ability to incorporate galactose-1-phosphate into nucleotide. This was revealed by assaying a microsample (biopsy) of his liver tissue using carbon-14-labeled galactose.

The rate of incorporation amounted roughly to about 2 to 5 percent of the normal activity in human liver samples (*27*). Likewise, administration of a small sample of carbon-14-labeled galactose *in vivo*, together with a glucuronide trapping agent (menthol), revealed that the same individual was able to incorporate a significant amount of galactose into menthol glucuronide (*28*). However, this incorporation was also low, amounting to 1 to 3 percent of normal. Red blood cells from the same individual did not show detectable amounts of activity of galactose-1-phosphate uridyl transferase. However, the method employed here is not as sensitive as that using carbon-14 labeled galactose.

It is not inconceivable that the liver might have had a total defect of the galactose-1-phosphate uridyl transferase and that it had gradually developed an alternate adaptive and closely related pathway. An adaptive mechanism might be expected to develop more readily in liver cells, which are, metabolically speaking, more universally active than, for instance, the more specialized erythrocytes. Perhaps age also plays a role. A liver biopsy sample from an infant with congenital galactosemia showed no trace of galactose-1-phosphate uridyl transferase (*27*).

It is unlikely that inhibitors are at work in this disease. Mixing hemolyzed erythrocytes from a nongalactosemic subject and a galactosemic patient did not significantly suppress the activity of the "normal" enzyme. Likewise, a case in which a galactosemic child was transfused with normal blood showed activity corresponding roughly to the amount of donor blood administered. In this case, the disappearance of the normal donor cells could be followed very well by the decrease in titer of galactose-1-phosphate uridyl transferase. It took 45 days to reach 50 percent of the original titer. This is somewhat faster than the time required to destroy 50 percent of a population of erythrocytes *in vivo* (*29*). A detailed study of more of such transfusion cases might throw additional light on the problem of the life span of erythrocytes *in vivo*. The possibility of anti-enzyme formation in such transfusion cases is being studied.

Galactosemia, a Hereditary Disease

That the defect in galactose-1-phosphate uridyl transferase is full-fledged at birth is apparent from the fact that blood from the umbilical cord of a newborn infant (one that had galactosemic siblings) had no detectable amounts of the transferase, whereas normal cord blood has abundant enzyme (*27*).

It might well be possible to pursue a study of the genetics of the disease using the erythrocyte enzyme assay. Preliminary experiments showed that neither of the parents of galactosemic children showed any striking decrease in enzyme activity. However, a moderate lowering of activity might be picked up. A genetic study was initiated by the important observations by Holzel and Komrower (*30*). The most pertinent fact in this study was that in the majority of the cases only one of the parents of galactosemic children showed a lowering of the galactose tolerance test.

Richard Post of the Institute for Human Variation, Columbia University, has suggested to me that the inheritance of the disease might be based on at least two multiple alleles. In other words, if A represents the normal gene and A' the state that affects galactose-1-phosphate metabolism, A'' is a third state giving another type of manifestation and aggravating the defect in galactose-1-phosphate metabolism if it is combined with A' such as $A'A''$. In that event, we should not only look for defects of galactose-1-phosphate uridyl transferase in galactosemic families, but also for another type of metabolic pattern that hitherto has escaped our attention as a trait in this disease.

Uridine Diphosphogalactose Pathway Dominating in Man

It should not be forgotten that there may be pathways of galactose metabolism totally different from the aforementioned uridine diphosphogalactose pathway operating in the animal body. A direct oxidation of free galactose has been described to occur in certain microorganisms (*31*). The latter mechanism seems, however, to be irreversible. Lactose synthesis seems also to follow different pathways (*32*) even in the same species, although it is considered most likely at present that both of these pathways operate through uridine diphosphogalactose. The biochemical symptoms in congenital galactosemia strongly indicate that in the growing infant the uridine diphosphogalactose pathway is the major one in operation.

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News of Science

NSF Summer Institutes for High-School and College Teachers

Approximately 4500 high-school and 250 college teachers of science and mathematics will participate during the summer of 1957 in teacher-training programs sponsored by the National Science Foundation at summer institutes in 95 colleges and universities throughout the United States and its territories. Total support of the program amounts to $4.8 million.

Eighty-six of the institutes will be open only to high-school teachers of science or mathematics; four will be open to both high-school and college teachers; and five will be for college teachers only. Six institutes offering a course in radiation biology just for high-school teachers are being jointly sponsored by the foundation and the Atomic Energy Commission.

Through its widely expanded summer-institute program for 1957, the foundation hopes to provide opportunities for teachers of science to cooperate in improving the quality of their teaching and to learn at firsthand of recent research progress in their respective fields. By this means more students with aptitude for science may be motivated toward careers in science, mathematics, and engineering through improvement of the quality of instruction they receive in high school. The foundation's program of summer institutes was initiated experimentally in the summer of 1953 with two institutes and the number of institutes was increased gradually to a point where the foundation supported 25 last summer.

Congress this year specified that $9.5 million of its appropriation to the foundation be used for the supplementary training of high-school teachers of science and mathematics. The summer institutes are in addition to the 16 academic-year institutes for which the foundation recently announced support in the amount of $4,065,000 and an expected enrollment of 750 high-school science and mathematics teachers. In both programs, teachers will pursue a course of study planned especially for them and conducted by leaders noted not only for competence in their fields but for skill in presentation.

The foundation grants to each summer institute will cover costs of tuition and other fees for a specified number of teachers—from 10 to 200, the average number to be approximately 50. Most institutes will pay stipends directly to participating teachers at the rate of $75 per week. Additional allowances and travel grants for dependents, to a maximum of four, are provided.

Inquiries and applications should be addressed to the director of summer institutes at one of the colleges listed here. Applications for the summer institute program must be submitted *by 1 Apr. 1957*.

For high-school teachers. Allegheny College, American University, Arizona State College, Atlanta University, Baylor University, Bucknell University, Clarkson College of Technology, Colorado College, Duke University, Iowa State College, Kansas State Teachers College, Louisiana State University, Marshall College (Huntington, W.Va.), Michigan State University, Morgan State College (Baltimore, Md.), Murray State College (Murray, Ky.), North Carolina College, Oak Ridge Institute of Nuclear Physics, Ohio University (Athens), Ohio Wesleyan University, Oklahoma Agricultural and Mechanical College, Rensselaer Polytechnic Institute, San Jose State College, South Dakota State College, Southern Methodist University, Stephen F. Austin State College (Nacogdoches, Tex.), Syracuse University, University of Alabama, University of Alaska, University of Arizona, University of Arkansas, University of California (Berkeley and Los Angeles), University of Hawaii, University of Idaho, University of Maryland, University of Minnesota (Duluth and Minneapolis), University of Mississippi, University of Missouri, University of North Carolina, University of North Dakota, University of Oklahoma, University of Pennsylvania, University of South Dakota, University of Texas, University of Wyoming, Virginia Polytechnic Institute, Wesleyan University, and Western Michigan College.

Biology only. Howard University, Indiana University, Iowa State Teachers College, Purdue University, and Rutgers University.

Radiation biology. (sponsored jointly with Atomic Energy Commission). Duke University, Harvard University, University of California (Los Angeles), University of New Mexico, University of Tennessee, and Wayne University.

Chemistry only. New Mexico Highlands University (Las Vegas), St. Louis University, Tufts University, Tuskegee Institute, University of California (Berkeley), University of New Hampshire, University of Rochester, University of Wisconsin, and Utah State Agricultural College.

Earth sciences only. Cornell University.

Mathematics only. Columbia University Teachers College, Indiana University, Miami University, Montana State College, Polytechnic Institute of Puerto Rico (San German, P.R.), State Teachers College (Oneonta, N.Y.; junior high-school teachers), State University of Iowa, University of Buffalo, University of Chicago, University of Colorado, University of Massachusetts, University of Notre Dame, and University of Wyoming.

Physics only. University of Vermont and Worcester Polytechnic Institute.

For high-school and college teachers. Claremont College, Montana State College, University of Washington, and University of Kansas.

For college teachers only. University of Oregon, Cornell University, University of North Carolina, University of Illinois (Urbana), and University of Colorado.

Orbit Computation

The establishment of two major programs for analyzing data and computing the orbit of the IGY earth satellite has been announced by Joseph Kaplan, chairman of the United States National Committee for the International Geophysical Year. The first program calls for the establishment by the Naval Research Laboratory of a computing and analysis center in Washington, D.C., to handle information provided by the radio tracking system. The second program calls for the establishment of a similar computing center by the Smithsonian Astrophysical Observatory at Cambridge, Mass., for data received from the optical and visual observation programs.

The problem of analyzing data and computing the orbit will have three aspects. The first will be gathering data on the satellite's motion during its first few revolutions and feeding these data into high-speed electronic computers. The results will establish an approximate satellite orbit, permitting observers throughout the world to train their instruments on the satellite, and also permitting the precision Schmidt cameras to make photographic measurements of the satellite's position. The second aspect will be to process the extensive subsequent data in order to compute the orbit accurately. The third aspect involves the analysis of the precise orbit data. Such analysis will yield important scientific information in a number of areas: the density of the upper atmosphere, possible calculations of the mass-distribution and shape of the earth through analyses of orbit perturbations, and geodetic determinations.

All three aspects of the problem require the use of high-speed electronic computers. In the acquisition period, speed is a very important factor if the further precise observations and determinations are to be undertaken promptly. In the precise orbit computation and data-analysis periods, large quantities of data requiring complicated, lengthy calculations are generated, requiring high-speed computing centers.

The Naval Research Laboratory has responsibility for the radio tracking program under the direction of John P. Hagen. The radio tracking system, called Minitrack, consists of a transmitter in the satellite issuing a 20 to 50 milliwatt signal at a frequency of 108 megacycles per second and a series of ground-station receivers using precision, multiple antenna arrays and extensive electronic installations. The expected precision of observations is about 3 minutes of arc under normal conditions, with improvement to a precision of 20 seconds of arc for observations at small zenith angles or for nighttime operation. A chain of ten stations, running principally north and south, is to be established. Present plans call for the following sites: Santiago and Antofagasta, Chile; Lima, Peru; Quito, Ecuador; Australia; Antigua, British West Indies; Havana, Cuba; Fort Stewart, Ga.; Washington, D.C.; and San Diego, Calif.

Data from these Minitrack stations and from others the U.S. National Committee for the IGY hopes other countries will establish, will be radioed to the Naval Research Laboratory computation center in Washington, D.C.

The Smithsonian Astrophysical Observatory has responsibility for the optical and visual observation programs under the direction of Fred L. Whipple. The most precise optical observations will be made using a modified Schmidt camera developed at the Smithsonian Astrophysical Observatory. Continuous strip film will simplify the problem associated with following the satellite. To provide accurate time, crystal clocks calibrated against station WWV will give a signal for photography simultaneous with the passage of the satellite and will provide a timing accuracy of one 0.001 second. Before the Schmidt cameras can be employed, however, the path of the satellite must be known to a precision of about 3 degrees. The radio system will provide this information, but to provide for the chance of radio failure in the satellite, a network of organized volunteer observers will be used. These teams will be stationed throughout the world in the satellite's latitude band width and will maintain a steady watch on the satellite.

The Schmidt precision camera program envisages the establishment of at least 12 stations around the world. Present plans call for the following sites: New Mexico, Florida, Spain, South Africa, Japan, Hawaii, Netherlands Antilles, Australia, and Argentina. Other sites in South America and in the Middle East are also under consideration. Data from these visual and optical-photographic programs will be relayed to the Smithsonian Astrophysical Observatory computation center at Cambridge, Mass., for analysis.

AAAS Resolution on Hungary

The AAAS Council adopted the following resolution concerning refugee Hungarian scientists when it met in New York on 30 Dec. 1956.

"Be it resolved that the American Association for the Advancement of Science join with the National Academy of Sciences–National Research Council in the expression of admiration and sympathy for fellow-scientists in Hungary. Be it further resolved that the facilities of the AAAS and its affiliated societies be employed to aid in the placement of refugee Hungarian scientific and technical personnel and to render such other assistance as may be appropriate."

British Physicians Demand Pay Increase

British physicians mobilized last month to press for higher pay in the National Health Service. For more than a year the Ministry of Health has rejected their demands.

About 35,000 general practitioners, hospital staff physicians, and consultants have asked for a 24 percent increase. At present the average practitioner receives the equivalent of $6250 a year, and a consultant about $10,000. This rate of income, based on the number of patients registered with a doctor, has not changed since 1952. The physicians have indicated that they may withdraw from the National Health Service, which was set up 8 years ago.

Cinematic Electron Diffraction

It is well known that a powder irradiated either by x-rays or by electrons will produce cones of diffracted radiations which, intersected by a photographic plate, appear as rings corresponding to the various planes that are reflecting the electrons or the x-rays in the crystal. Because of this circular symmetry it is possible to use a slit that effectively cuts out just one diameter in the diffraction rings. By evaluating the intensities of the various reflections across this diameter, it is possible to determine the structure.

Boettcher first pointed out that if the

photographic plate is moved normally to the slit, then the undiffracted primary beam is marked as a sharp dark line, and the diffracted beams appear on both sides of this line. This permits the investigation of the diffraction pattern as a function of time. If oxidation, for instance, or a change in structure due to temperature changes or other changes in the material takes place, this can be made visible at once.

This method, which was first described by Boettcher, is now described in detail by R. Thun, [*Umschau* **56**, 660 (1 Nov. 1956); **56**, 688 (15 Nov. 1956)]. As an example, the behavior of a cobalt layer which has been evaporated is studied as a function of temperature; as the temperature is increased it shows first a strongly disturbed lattice, then an unstable intermediate state, the beginning of the hexagonal phase, and finally the beginning of the cubic phase.

By evaporating a layer of copper and antimony it is possible to follow as a function of temperature and time the transformation of the superposition of the copper and antimony lattice into a lattice of Cu_2Sb. In a similar way, by using a magnesium layer it is possible to investigate the changes which take place under oxidation and which show first only the reflections of magnesium and then the reflections due to the newly developed magnesium oxide lattice. This method, therefore, while extremely simple, has great possibilities for the practicing metallurgist.—K. L.-H.

News Briefs

■ The United Kingdom now expects to produce more than twice as much electricity from nuclear reactors by 1965 as was estimated prior to the starting of the first reactor at Calder Hall. The greater part of the gain in output is expected to be derived from improvements in the design of reactors of the gas-cooled, graphite-moderated type such as that at Calder Hall. The Central Electric Authority is reported to be considering further increase by building 15 new nuclear power stations instead of 12 as originally planned. The twelve stations planned at first were expected to have an output of 1.5 to 2 million kilowatts; design improvements lead to estimates of 3 to 4 million kilowatts.

■ Exploration for uranium in Mexico will get under way in 1957 under the auspices of the Mexican Government, according to the National Nuclear Energy Commission. The search will be under the direction of government geologists who have studied uranium mining techniques in Colorado and Europe. It will begin in the northwestern state of Chihuahua and in the southern state of Oaxaca, where radioactive rocks have previously been noted.

Whether a commercial concentration of uranium exists is not yet known, but the potential participation of foreign capital already is a big issue. A law reserving all uranium found in Mexico for national ownership has been passed. However, the National Nuclear Energy Commission is studying the possible use of private capital, and presumably foreign capital, under government contracts.

■ According to a press report, Nikolai Semyonov, director of the Institute of Chemistry of the Soviet Academy of Science, and Nobel laureate in chemistry jointly with Sir Cyril Hinshelwood, stated, when he was in Stockholm to receive the Nobel prize, that the death of Stalin had meant the liberation of Soviet science. He further said that Soviet scientists were no longer compelled to follow a dogmatic line.

Scientists in the News

The semimonthly journal *Modern Medicine* has announced its 1957 awards for distinguished achievement. The 10 American physicians and research scientists honored are as follows:

JEROME W. CONN, professor of internal medicine and director of endocrinology and metabolism, University of Michigan Medical School, for "furthering the knowledge of endocrinology and elucidating the clinical significance of aldosterone in health and disease."

MICHAEL E. DEBAKEY, Judson L. Taylor professor of surgery and chairman of the surgery department, Baylor University College of Medicine, for "making aortic resection a safe procedure and for his work on replacement of vascular defects with homografts and plastic bridges."

VINCENT DU VIGNEAUD, professor and head of biochemistry, Cornell University Medical College, for "continuous and brilliant studies of the structure of biologically active sulfur-bearing organic compounds and for his synthesis of oxytocin."

JULIUS LEMPERT, surgical director of Lempert Institute of Otology in New York, research professor of otology at Tufts College Medical School, and visiting lecturer in otolaryngology at the University of Pennsylvania Graduate School of Medicine, for "clinical investigations leading to relief of deafness and to the advancement of otology."

CHARLES W. MAYO, head of a section of surgery in the Mayo Clinic and professor of surgery at the University of Minnesota Mayo Foundation Graduate School, for "service to Medicine and mankind through leadership and distinguished statesmanship in the councils of the United Nations."

EDWIN E. OSGOOD, professor of medicine and head of the division of experimental medicine, University of Oregon Medical School, for "outstanding achievements in hematology and for excellent work in the use of radiophosphorus in the treatment of leukemia."

TOM D. SPIES, professor of nutrition and metabolism and chairman of the department, Northwestern University Medical School, for "pioneering in the management of deficiency diseases and for his untiring investigations in the wide field of clinical nutrition."

BENJAMIN SPOCK, professor of child development, Western Reserve University, for "inspiration and aid he has given to the mothers of America in developing and expounding a sensible approach to child development and child psychology."

EUGENE A. STEAD, JR., professor of medicine at Duke University School of Medicine, for "distinction as a stimulating teacher and as an investigator of the mechanisms of heart failure and of water and salt balance."

DONALD D. VAN SLYKE, research chemist with Brookhaven National Laboratory, Upton, N.Y., for "creation of methods of chemical analysis in the service of medicine and for the profound influence his work has had on diagnosis and treatment."

JOHN VON NEUMANN has received the American Meteorological Society's award for extraordinary scientific accomplishment. He was honored "for his farsighted contribution to the science of meteorology and the national interests in developing the modern, high-speed electronic computer with meteorological application as an ultimate aim, and for his support and encouragement in organizing the world's first research group in numerical weather prediction."

THORNDIKE SAVILLE, dean of the College of Engineering at New York University, will retire at the beginning of the autumn term in 1957. Saville became professor of hydraulic and sanitary engineering at N.Y.U. in 1932 and was made dean in 1935. After retirement he plans to act as a consultant in hydrology and coastal engineering.

ERNEST OPIK of Armagh Observatory, Armagh, Northern Ireland, has an appointment as visiting research professor in the physics department at the University of Maryland for the academic year 1956–57. HIROOMI UMEZAWA of the University of Tokyo is serving as visiting lecturer in the same department through the first 3 months of 1957.

CHARLES KITTEL, professor of physics at the University of California, Berkeley, has been awarded this year's $1000 Oliver Buckley solid-state physics prize for his applications of magnetic resonance methods to investigations of the electronic solids. The award, which is administered by the American Physical Society, was established by the Bell Telephone Laboratories in honor of one of its last presidents.

ALWIN M. PAPPENHEIMER, JR., who has been on the staff of New York University College of Medicine since 1941, has been appointed professor and chairman of the department of microbiology of that institution. He succeeds COLIN M. MACLEOD, who has become John Herr Musser professor of research medicine and chairman of the department of research medicine at the University of Pennsylvania School of Medicine.

ALLAN B. CRUNDEN, JR., of Montclair, N.J., has been appointed editor-in-chief of the *Journal of Astronautics*, official organ of the American Astronautical Society, 516 Fifth Ave., New York 36, N.Y.

GREGORIO OCLANDER, a pediatrician, has joined the medical research cooperation division of Eli Lilly and Company. He will participate in Lilly's export program related to the areas of pediatric medicine, vitamins, and nutritional factors; he also will contribute to Lilly's Latin American publications. A native of Argentina, Oclander was head of pediatrics and subdirector of Moron's Hospital in Buenos Aires before coming to the United States in 1953.

EVELYN L. OGINSKY, formerly research associate at the Merck Institute for Therapeutic Research, Rahway, N.J., has joined the University of Oregon's Medical School as associate professor of bacteriology.

Recent Deaths

EDWIN P. ADAMS, Walpole, Mass.; 78; emeritus professor and former chairman of the physics department at Princeton University; 31 Dec.

OLIVER L. DAVIS, Morristown, N.J.; 60; retired chemist; 27 Dec.

ROBERT ELMAN, St. Louis, Mo.; 57; professor of clinical surgery at Washington University; 23 Dec.

HENRY V. B. ERBEN, Schenectady, N.Y.; 58; retired executive vice president of the General Electric Company; 26 Dec.

FRED S. FRANKFURTER, White Plains, N.Y.; 76; retired pharmacist and trustee emeritus of the College of Pharmacy of Columbia University; 1 Jan.

WILLIAM B. GERY, Norwalk, Conn.; 60; technical director of the Dorr-Oliver Company; 1 Jan.

GWENDOLEN S. JONES, New York, N.Y.; 53; instructor in medicine at Columbia University; 30 Dec.

ROY L. LANGDON, Philadelphia, Pa.; 64; associate professor of medicine at Temple University; 22 Dec.

EDWIN F. LOWRY, Danvers, Mass.; 65; manager of the research engineering laboratories of the lighting division of Sylvania Electric Products; 2 Jan.

WILLIAM B. MELDRUM, Haverford, Pa.; 69; professor emeritus of chemistry and former chairman of the department at Haverford College; 31 Dec.

RANDOLPH G. PACK, Greenwich, Conn.; 66; forest conservationist and president of the Charles Lathrop Pack Forestry Foundation; 25 Dec.

ARTHUR PARRETT, New York, N.Y.; 60; vice president and director of research for Rayonier, Inc.; 28 Dec.

SAMUEL SHIENERNAN-SHARON, New York, N.Y.; 58; vice president of the Ions Exchange and Chemical Corporation of New York; 31 Dec.

JOZSEF VARGA, Budapest, Hungary; 66; professor of technical sciences in the Universities of Budapest and Veszprem; announced in Budapest on 29 Dec.

Education

■ A course of study to train science and fiscal writers is now under consideration at the Columbia University Graduate School of Journalism, according to Edward W. Barrett. Adding a second year to the curriculum, the course would be designed for the writer "who has already moved along in his profession" and would help meet the present "severe shortage" of newspapermen qualified to write on science, business, and finance. Some provision for financial assistance to students would be made.

Students would be protected from aimless sampling, Barrett said. "Rather, under the guidance of a senior scholar and a mature journalist, each would be assisted in applying himself to a single field, doing so in a journalistic context, and producing finally a work of journalistic merit—be it a major magazine article, a script for a television series, or a small book.

Also under consideration is a course designed to introduce the principles of journalism and the American way of life to foreign newspaper students who expect to return abroad, Barrett added. At present, few foreigners attend the School of Journalism because the curriculum heavily emphasizes English-language writing. "The proposed curriculum would involve some courses taken jointly with American students, plus studies in American civilization, economy and the ethics and principles of free journalism," Barrett said.

■ A research training program to increase scientific manpower for clinical and nonclinical cancer research has been established by the National Cancer Institute, Bethesda, Md., with $1.2 million appropriated for the program by Congress. The first group of grants, amounting to $819,067, will be awarded to 14 institutions whose applications were recommended by the National Advisory Cancer Council.

The program extends and supplements but does not replace the research training opportunities available through regular research fellowships and through employment on research projects. Under the new program the institutions receiving funds select and appoint the individuals to be trained and determine the stipends they are to be paid.

Slightly more than half of the $1.2 million was appropriated especially for training in fields of chemotherapy and steroid hormones. The research fields represented by the current awards are cancer chemotherapy, steroid biochemistry, research medicine, pharmacology, biochemistry, immunology, research surgery, histochemistry, electron microscopy, genetics, cytology, radiobiology, and cancer biology.

The following grants for training in chemotherapy and steroid horomones were announced: University of Utah, $74,145; Clark University, $97,761; Columbia University, $52,812; Yale University, $37,800; Sloan-Kettering Institute for Cancer Research, $100,000; Roswell Park Memorial Institute, $32,616.

Other research training grants have been awarded to: University of Wisconsin, $45,792; University of Minnesota, two grants of $50,000 each; University of Kansas, $38,802; Brown University, $52,380; Stanford University, $50,000; Washington University, $11,577; Roscoe B. Jackson Memorial Laboratory, $75,000; Massachusetts General Hospital, $50,382. Requests for information concerning this program should be addressed to the Research Grants and Fellowships Branch, National Cancer Institute, Bethesda 14, Md.

■ The University of Michigan has tentatively accepted gifts of 210 acres and $6.5 million from the Ford Motor Company and the Ford Motor Company Fund to be used in establishing a Dearborn Center of the university, which has a projected enrollment of more than 2700 students. Acceptance depends on appropriation by the state legislature of the necessary operating funds. The combined

gifts are the largest ever made by a company and its charitable fund to an educational institution. The land offered includes Fair Lane, the former estate of Henry Ford; the $6.5 million will pay for buildings. The Dearborn Center would provide the university with a major opportunity to develop an educational system that combines classroom and shop instruction with practical work in industry. In addition to both undergraduate and graduate engineering and business administration courses, the center would offer junior and senior programs in liberal arts and sciences. No student housing is planned at present, since it is expected that most of the students will live within commuting distance.

■ The Rehabilitation Center of the Hospital of the University of Pennsylvania is to be enlarged and remodeled to increase its services to disabled and physically handicapped persons and its facilities for teaching and research in rehabilitation. This construction program will double the center's present floor space. Work will start immediately and probably be completed in 8 months.

Cost of the project will approximate $450,000. Of this sum, two-thirds was contributed by individuals and organizations interested in rehabilitation, and one-third was obtained from Federal sources under the Hill-Burton Act, through approval by the Commonwealth of Pennsylvania hospital construction authority. Hill-Burton funds must be matched two-for-one by the grant recipient.

The center will be named in honor of George Morris Piersol, dean of the Graduate School of Medicine and professor emeritus of physical medicine and rehabilitation. This medical specialty has been Piersol's interest for many years. He was the first chairman of the university's Rehabilitation Commission.

Grants, Fellowships, and Awards

■ The National Council to Combat Blindness, Inc., in accordance with its program concerned with the financing of research in ophthalmology and the related sciences, has announced that applications for its 1957–58 Fight for Sight grant-in-aid and fellowship awards will be considered at the eighth annual meeting of the organization's Scientific Advisory Committee that is to be held in the spring. The closing date for receipt of completed applications for grant-in-aid and fellowship awards is *15 Apr.* Applications for summer-student fellowships will be reviewed in advance of the meeting, and such applications should be filed with the office of the organization no later than *1 Apr.*

All applicants are required to make their own arrangements for suitable research facilities with accredited institutions. Appropriate application forms may be obtained by addressing: Secretary, National Council to Combat Blindness, Inc., 30 Central Park South, New York 19, N.Y.

■ The U.S. Public Health Service has announced approval of 73 grants, totaling $24,460,467, to help institutions in 24 States and the District of Columbia build additional health research facilities. The awards were approved by the Surgeon General upon recommendation of the National Advisory Council on Health Research Facilities.

The new grants are the second group of awards under a new program enacted by the Congress late in its last session. The legislation authorized distribution of $30 million a year for 3 years; it also established the Health Research Facilities Council. At its first meeting in September the council recommended seven grants totalling $765,159. The next meeting of the council is scheduled for March at the National Institutes of Health in Bethesda, Md., when grant applications will again be reviewed.

■ The Albert and Mary Lasker Foundation, Chrysler Building, New York 17, N.Y., has announced the opening of the eighth annual Albert Lasker medical journalism awards competition. The awards will be presented to the newspaper writer and magazine writer who have written during 1956 the best articles, series of articles, editorials, or columns dealing with the improvement of public health or the prolongation of life through medical research or public health programs. A radio-television award will be presented to the best program or series of programs in this field broadcast over a station or network during 1956. The deadline for entries will be *11 Feb.*

Inaugurated in 1949, the three awards have been increased this year from $1000 to $2000 each. Included with each award is a citation and a silver statuette of the Winged Victory of Samothrace, symbolizing victory over death and disease.

A committee of journalists, laymen, and physicians will act as judges. Articles and scripts will be rated on the basis of accuracy, significance, timeliness and proficiency in the translation of technical information into lay language, and skill in arousing and holding the average person's interest. The foundation seeks especially to recognize journalism that contributes to a better public understanding of medical research and health programs relating to the diseases that are major causes of death or disability—especially heart diseases, cancer, mental illnesses, arthritis, blindness, and neurological diseases.

Miscellaneous

■ A progress review of the U.S. Geological Survey's investigation of radioactive deposits in the United States and Alaska between 1 June and 30 Nov. 1955 has just been made available through the Office of Technical Services, U.S. Department of Commerce. Reports in the 340-page volume reflect emphasis by the Geological Survey on the understanding of geologic conditions favorable for concentration of uranium, rather than on the search for specific minable deposits. This semiannual report, TEI-590 *Geologic Investigations of Radioactive Deposits,* U.S. Department of the Interior Geological Survey for the U.S. Atomic Energy Commission, Dec. 1955, may be ordered from OTS, U.S. Department of Commerce, Washington 25.

■ The Thomas Alva Edison Foundation, Inc., presented its second annual National Mass Media awards last month. Among those of special interest to scientists were the following: to the movie *On the Threshold of Space* (Twentieth Century Fox) as "the best science film for youth" for 1956; to *Adventures in Science* (CBS) as "the best radio program for youth" for 1956.

A special citation of merit was made to New York City's municipal broadcasting station, WNYC, for its first annual "Science Seminar," which carried more than 30 talks on the general subject of "The growing shortage of scientists and engineers." Among the titles were: "An inventor looks at education," "Toward peaceful uses of the atom," and "Encouraging scientific talent."

■ A new quarterly journal, the *IBM Journal of Research and Development,* is being published quarterly by the International Business Machines Corporation, 590 Madison Ave., New York 22, N.Y. The first issue was released on 1 Jan. Purposes of the journal are to publish original work by IBM scientists and engineers for the largest possible audience of interested technical people, and to help promote more rapid dissemination of scientific and technical information within American industry and throughout the world.

The new magazine will publish comprehensive articles on the latest scientific and technical results from IBM research and development laboratories here and abroad. Articles will come from fields as varied as solid-state physics, chemistry, metallurgy, information theory, and electronics. Other articles will treat the latest developments in computers, data-processing machines, and design of components such as magnetic core memories and semiconductor devices. The journal is available by subscription at a cost of $3.50 per year.

Reports

Defect in Uptake of Galactose-1-Phosphate into Liver Nucleotides in Congenital Galactosemia

As stated previously (*1*), α-galactose-1-phosphate (Gal-1-P) (*2*) is incorporated into uridine nucleotides through the reaction (step 2, *1*)

$$\text{Gal-1-P} + \text{UDPG} \rightleftharpoons \text{G-1-P} + \text{UDPGal}$$

The enzyme that catalyzes this reaction is called galactose-1-phosphate uridyl transferase. The subsequent reaction (step 3, *1*)

$$\text{UDPGal} \rightleftharpoons \text{UDPG}$$

is catalyzed by an enzyme that is now called uridine diphosphogalactose 4-epimerase (*1*). Finally, the reaction (step 4, *1*)

$$\text{UDPG} + \text{PP} \rightleftharpoons \text{UTP} + \text{G-1-P}$$

is catalyzed by the enzyme uridine diphosphoglucose pyrophosphorylase.

It was recently reported (*3–5*) that lysed erythrocytes from subjects afflicted with congenital galactosemia show a striking defect in galactose-1-phosphate uridyl transferase (the enzyme of step 2, *1*). Since the liver is the organ of the body which carries the major burden of galactose metabolism, it was considered of special interest to study some of the afore-mentioned enzymes in this tissue, particularly to see whether the liver tissue of galactosemic subjects showed the same defect in galactose-1-phosphate uridyl transferase.

The assay to be used for fresh homogenates of liver had to be modified significantly from that used for blood (*4*), for neither of the reaction products formed by step 2 could be assayed enzymatically in the liver preparations. The most important reaction product, uridine diphosphogalactose (UDPGal), is immediately converted to uridine diphosphoglucose (UDPG) because liver contains large amounts of uridine diphosphogalactose 4-epimerase and its cofactor, diphosphopyridine nucleotide (*6*). Moreover, although α-glucose-1-phosphate (G-1-P) and glucose-6-phosphate may to some extent accumulate, the liver homogenates usually contain much higher concentrations of these esters than would be expected to be liberated in step 2, and the blanks are therefore very high.

An alternative method was therefore employed. This is based on the principle that galactose-1-phosphate can be separated from even minute amounts of uridine diphosphogalactose (or other nucleotides) by a microscale fractionation with norite (*7*). At *p*H 3, norite will adsorb the nucleotide but not the phosphate ester; the nucleotide can subsequently be eluted efficiently from the washed norite with 50-percent ethanol containing 0.1 percent ammonia. If C^{14}-labeled galactose-1-phosphate is used, the incorporation of radioactivity into the nucleotide fraction can be measured and this specific metabolism of the sugar phosphate thus determined.

Carbon-14 labeled galactose-1-phosphate was prepared from 1-C^{14}-galactose by using purified yeast (galactose-adapted *Saccharomyces fragilis*) galactokinase (*8*) and adenosine triphosphate (*9*). Uridine diphosphoglucose was obtained from Sigma Chemical Company and from Pabst Laboratories.

Liver biopsy or autopsy samples (*10*) ranging from 20 to 200 mg were ground to a pulp in a micro mortar and extracted with 0.1*M* phosphate buffer at *p*H 7.4. The samples were either fresh tissue or tissue that had been frozen immediately after removal and kept in a frozen state until analysis (*11*).

The incubation mixture contained 0.15 μmole of 1-C^{14}-galactose-1-phosphate (S.A., 500,000 count/min μmole, 0.5 μmole of uridine diphosphoglucose, 1.25 μmole of uridine triphosphate (UTP) (to recycle the glucose-1-phosphate formed in the reaction into uridine diphosphoglucose synthesis), and cysteine (6 μmoles), Mg^{++}, and phosphoglucomutase to pull the reaction by further oxidation of the glucose-1-phosphate formed. The incubation was run in 0.1*M* glycine buffer at *p*H 8.7; liver tissue equivalent to 7 to 15 mg was used. The control sample was identical except for the absence of labeled galactose-1-phosphate, which was added after deproteinization. The samples were incubated at 37°C for 30 minutes and deproteinized by heating at 100° for 2 minutes. In some cases, an additional control was made by incubating labeled galactose-1-phosphate with the liver tissue in the absence of uridine diphosphoglucose. In this sample, there was some incorporation by normal liver tissue because of the uridine diphosphoglucose present in the tissue or formed from the uridine triphosphate added.

In two cases in which the liver had been frozen before analysis, uridine diphosphoglucose pyrophosphorylase (pyrophosphate uridyl transferase) activity in the tissue was also estimated (step 4, *1*). Phosphorus-32 labeled glucose-1-phosphate (0.3 μmole; S.A., 140,000 count/min μmole) was incubated with 0.75 μmole of uridine triphosphate in the presence of 15 mg of liver tissue. The incubation was run in 0.1*M* tris buffer at *p*H 7.5, and the mixture also contained ammonium sulfate (final concentration 0.1*M*) to inhibit the conversion of glucose-1-phosphate to glucose-6-phosphate, and inorganic pyrophosphatase to pull the reaction in the direction of uridine diphosphoglucose synthesis. The incubation was run for 30 minutes at 37°C and the mixture was then deproteinized with heat. The control sample lacked P^{32}-labeled glucose-1-phosphate, which was added after deproteinization.

The nucleotides in the deproteinized sample were adsorbed on 45 mg of norite by exposure at *p*H 3 for 30 minutes. The norite was washed twice with 10 ml of 0.001*N* HCl and twice with 10 ml of water and then eluted with 5 ml of ammoniacal 50-percent ethanol for 30 minutes. The eluate was evaporated down to a small volume, and aliquots were assayed for radioactivity. The ethanol eluates of washed norite contain very little dry material, and there is thus no appreciable self-absorption.

The results are given in Table 1, ex-

Table 1. Uridyl transferases in human liver homogenates (micromoles incorporated into nucleotide per gram of liver, per hour).

Subject	C^{14}-labeled Gal-1-P	P^{32}-labeled G-1-P
Nongalactosemic adult*	> 15.0	
Nongalactosemic infant*	> 25.00	> 4.0
Galactosemic adult, biopsy	1.2	
Galactosemic infant, biopsy	< 0.3	> 3.0

* Post mortem.

All technical papers and comments on them are published in this section. Manuscripts should be typed double-spaced and be submitted in duplicate. In length, they should be limited to the equivalent of 1200 words; this includes the space occupied by illustrative or tabular material, references and notes, and the author(s)' name(s) and affiliation(s). Illustrative material should be limited to one table *or* one figure. All explanatory notes, including acknowledgments and authorization for publication, and literature references are to be numbered consecutively, keyed into the text proper, and placed at the end of the article under the heading "References and Notes." For fuller details see "Suggestions to Contributors" in *Science* 125, 16 (4 Jan. 1957).

Table 2. Galactose-1-phosphate uridyl transferase in blood cell hemolysates (micromoles of uridine diphosphoglucose utilized per milliliter of red blood cells, per hour, *4*).

Subject	Enzymatic activity
Normal adult	1.0 to 3.0
Normal infant (cord blood)	2.0
Galactosemic adult	< 0.02
Galactosemic infant (cord blood)	< 0.02
Galactosemic infant transfused with normal blood	
First day	0.50
40th day	0.24
200th day	0.01

pressed as micromoles of galactose-1-phosphate or glucose-1-phosphate incorporated per gram of liver, per hour. It can be seen that the galactose-1-phosphate uridyl transferase of liver is greatly lowered in congenital galactosemia. In one case, an infant afflicted with the disease, no detectable incorporation of 1-C^{14}-galactose-1-phosphate took place (less than 0.5 percent); the analogous transferase incorporating pyrophosphate (uridine diphosphoglucose pyrophosphorylase) was, however, present. In another case, an adult with the disease, there was a slight but definite ability to incorporate 1-C^{14}-galactose-1-phosphate into uridine nucleotides. The rate amounted to about 5 percent of the average normal rate. Differences in the severity of the disease may thus be reflected in the completeness of the metabolic defect in liver tissue. This patient has previously been found, clinically, to manifest some tolerance for galactose. The estimate here is in fair agreement with some metabolic *in vivo* studies performed on the same subject (*12*). Whether the result found is due to a slight activity of galactose-1-phosphate uridyl transferase or to an alternate, related pathway (compare *13*) that is at present unknown cannot be decided by this technique. Neither uridine diphosphoglucuronic acid nor uridine triphosphate produced the same incorporation of 1-C^{14}-galactose-1-phosphate as did uridine diphosphoglucose in liver tissue from this patient. It should be noted that the same adult patient showed no detectable galactose-1-phosphate uridyl transferase in red cell hemolysates that were incubated with galactose-1-phosphate and uridine diphosphoglucose (see Table 2).

In the case of uridine diphosphoglucose pyrophosphorylase, the values are minimized by appreciable hydrolysis of both reactants in the homogenates; the levels of activity given for this enzyme are therefore undoubtedly much underestimated. In addition, uridine diphosphoglucose may be broken down or may undergo exchange with unlabeled glucose-1-phosphate in the homogenates, and incorporation into the nucleotide fraction may therefore be decreased. This would affect the values for both enzymes. However, the activity of galactose-1-phosphate uridyl transferase in galactosemic liver is still clearly only a small percentage of that in nongalactosemic tissue.

Table 2 gives the results of some further studies on galactose-1-phosphate uridyl transferase in red cell hemolysates. One infant with galactosemia was transfused with normal red cells because of bleeding tendencies; this offered an opportunity to follow the disappearance of donor erythrocyte galactose-1-phosphate uridyl transferase. A half-life of about 40 days was found.

As can be seen, the assay can be applied to umbilical cord blood of newborn infants, and the defect is also present in cord blood of galactosemic infants (*14*). This observation indicates that the disease can be diagnosed at birth and that the proper treatment can be instituted immediately without ever subjecting these patients to the deleterious effects of galactose or milk ingestion.

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2. Abbreviations: G-1-P, α-glucose-1-phosphate; Gal-1-P, α-galactose-1-phosphate; PP, inorganic pyrophosphate; UDPG, uridine diphosphoglucose; UDPGal, uridine diphosphogalactose; UTP, uridine triphosphate.
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9. Pure 1-C^{14}-galactose was kindly supplied by Horace Isbell, National Bureau of Standards. Yeast galactokinase was made available to us through the courtesy of R. O. Brady, Jr., and R. M. Burton, National Institute of Neurological Diseases and Blindness.
10. Liver biopsies from galactosemic subjects were obtained through the courtesy of W. Bergren and G. N. Donnell, Children's Hospital, Los Angeles, Calif., and Lennard Gold, National Cancer Institute. Autopsy material was obtained through the courtesy of Richard K. Swarm, National Cancer Institute.
11. Grateful acknowledgment for excellent technical assistance is made to Bodil Waage-Jensen, trainee under the American Scandinavian Foundation through a grant-in-aid to one of us (H. M. K.) by the Eli Lilly Laboratories.
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14. The galactosemic cord blood analyzed was sent to us by Fred I. Dorman, Lakeland, Fla.

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14 November 1956

Enzyme Formation in Galactose-Negative Mutants of Escherichia coli

Morse, Lederberg, and Lederberg recently reported the transduction of Gal+ genes from galactose-positive to galactose-negative cells of *Escherichia coli* strain K-12 by the bacteriophage lambda (*1*). They also described the transduction of Gal– genes from galactose-negative to galactose-positive cells (*2*). This report (*3*) deals with the correlation between the various galactose loci and the formation of galactose-metabolizing enzymes.

Galactose (Gal) (*4*) is metabolized by *E. coli* adaptively much as it is by *Saccharomyces fragilis* (*5*) through α-galactose-1-phosphate (Gal-1-P), uridine diphosphogalactose (UDPGal), and uridine diphosphoglucose (UDPG) as follows:

$$\text{Gal}^* + \text{ATP} \xrightarrow{\text{Galactokinase}} \text{Gal}^*\text{-1-P} + \text{ADP} \quad (1)$$

$$\text{Gal}^*\text{-1-P} + \text{UDPG} \underset{\text{Gal-1-P uridyl transferase}}{\rightleftharpoons} \text{UDPGal}^* + \text{G-1-P} \quad (2)$$

$$\text{UDPGal}^* \underset{\text{UDPGal-4-epimerase}}{\rightleftharpoons} \text{UDPG}^* \quad (3)$$

The sum of reactions 1, 2, and 3 is

$$\text{Gal} + \text{ATP} \longrightarrow \text{G-1-P} + \text{ADP}$$

As is shown in these equations, it is necessary that the three enzymes in steps 1, 2, and 3 operate in order to convert free galactose to a glycolytic intermediate. The catalytic amount of uridine diphosphoglucose needed for this conversion could be supplied by another enzyme, uridine diphosphoglucose pyrophosphorylase, as follows:

$$\text{UTP} + \text{G-1-P} \underset{\text{UDPG pyrophosphorylase}}{\rightleftharpoons} \text{UDPG} + \text{PP} \quad (4)$$

Galactokinase activity was measured by determining the amount of galactose-1-phosphate formed during the incubation of galactose and adenosine triphosphate (ATP) with the enzyme solution. The galactose-1-phosphate formed was measured by the reduction of triphosphopyridine nucleotide in a coupled re-

action of purified galactose-1-phosphate uridyl transferase, glucomutase, and *Zwischenferment* (*6*). Galactose-1-phosphate uridyl transferase activity was measured by determining spectrophotometrically the reduction of triphosphopyridine nucleotide in a coupled reaction with phosphoglucomutase and *Zwischenferment* (*7*). Uridine diphosphogalactose 4-epimerase activity was measured by determining diphosphopyridine nucleotide reduction spectrophotometrically in a coupled reaction with uridine diphosphoglucose dehydrogenase (*8*). Uridine diphosphoglucose pyrophosphorylase activity was measured in the same way as galactose-1-phosphate uridyl transferase assay except that pyrophosphate was substituted for galactose-1-phosphate (*7*).

The mutants of *E. coli* K-12 were grown in 300 ml of glycerol-complete medium [10 g of casein digest (NZ case), 5 g of yeast extract, 3 g of K_2HPO_4, 1 g of KH_2PO_4, and 5 g of glycerol per liter] for 12 to 16 hours at 37°C (*9*). After harvest by centrifugation, the cells were resuspended in 300 ml of galactose-complete medium (as described in the previous sentence except that galactose was substituted for glycerol) and incubated for 6 to 10 hours at 37°C. The crude cell-free extracts were prepared by grinding the washed cells with alumina powder or by disintegration in a mechanical cell disintegrator (*10*).

The distribution of the four enzymes concerned with galactose metabolism in the galactose mutants of *E. coli* is summarized in Table 1. On the basis of this table, the mutants that were tested can be classified into two groups: one lacks galactose-1-phosphate uridyl transferase and the other lacks galactokinase. Uridine diphosphogalactose-4-epimerase and uridine diphosphoglucose pyrophosphorylase were present in all the mutants tested. In fact, the latter two enzymes are not induced enzymes because they are present in the cells grown on glycerol synthetic medium without previous induction to galactose (*11*).

An observation, which may be noteworthy, is the fact that the loci which are all concerned with the development of galactokinase activity are not located in the same cluster of genes. As reported by Morse, Lederberg, and Lederberg (*1, 2*), the galactose loci, Gal_1 to Gal_8 (W3091 to W3097 and W3178) are closely linked to one another, whereas the Gal– locus in the mutant W3142 is separated from the afore-mentioned cluster of genes and not closely linked to the phage lambda. It appears from Table 1 that the loci Gal_2, Gal_8, and the more distant Gal– locus of W3142 are all involved in the development of galactokinase activity.

In order to confirm these results by an independent technique, experiments with C^{14}-labeled galactose were carried out. The principle of these experiments was that extracts lacking either galactokinase or galactose-1-phosphate uridyl transferase would fail to incorporate free galactose-1-C^{14} into uridine nucleotides, as indicated by the asterisks in Eq. 1, 2, and 3. If, however, the extracts of a mutant in group 1 and of another in group 2 are mixed, the incorporation of free galactose-1-C^{14} into uridine nucleotides should take place.

One micromole of galactose-1-C^{14} (2.25×10^5 count/min μmole) (*12*), 1.7 μmole of adenosine triphosphate, 5 μmole of $MgCl_2$, 100 μmoles of tris buffer (*p*H 7.5), 0.3 μmole of uridine diphosphoglucose, 25 μmole of NaF, 10 μmole of cysteine, and 0.1 ml of crude extract of *E. coli* (about 1 mg of protein) in a total volume of 1.0 ml were incubated for 1 hour at 37°C. After the reaction had been stopped by heating the reaction mixture at 100°C for 1.5 minutes, the nucleotides were adsorbed on charcoal and treated as described by Kalckar *et al.* (*13*).

The results of these experiments are presented in Table 2. The first part of the table shows the results obtained with unmixed extracts of single mutants, and the second part of the table presents the results obtained with mixtures of the extracts of two different mutants. It should be noted that the mixture of extracts of two mutants which lack the activity of the same enzyme failed to show any incorporation of free galactose into uridine nucleotides, whereas the mixture of extracts of two mutants which lack the activity of galactokinase and galactose-1-phosphate uridyl transferase, respectively, showed the incorporation of free galactose at the level observed with the extract of the Gal+ mutant.

These results not only confirmed the conclusions derived from Table 1, but also ruled out the possibility that the inactivity of galactokinase or galactose-1-phosphate uridyl transferase is the result of the presence of some inhibitor in the extracts of these mutants. It cannot be decided at this point whether the lack of the enzymatic activity observed in these mutants is due to a complete loss of the ability to form the enzyme protein molecule or whether it is due to the formation of an incomplete enzyme protein molecule as in the *Neurospora* mutants that have defects in tryptophan synthesis, as described by Yanofsky (*14*).

Table 2. Incorporation of galactose-1-C^{14} into uridine nucleotides by extracts of *E. coli* mutants.

Strain	Genetic notation	Additions of extracts (ml)										
		Single extract					Mixed extract					
W3100	Gal+	0.1										
W3091	Gal_1–		0.1				0.1	0.1	0.1			
W3094	Gal_4–			0.1			0.1			0.1	0.1	
W3092	Gal_2–				0.1			0.1		0.1		0.1
W3142	Gal–*					0.1			0.1		0.1	0.1
Total counts† incorporated into uridine nucleotides (10^{-6} count/min)		33.9	0	0	0	0	0	37.6	36.2	29.6	39.0	0

* See the footnote of Table 1. † The counts have been corrected for the control, the reaction of which was stopped at zero time.

Table 1. Distribution of the enzymes metabolizing galactose in *E. coli* mutants.

Strain	Genetic notation	Galactokinase	Gal-1-P uridyl transferase	UDPGal-4-epimerase	UDPG pyrophosphorylase
W3100	Gal+	+	+	+	+
W3091	Gal_1–	+	–	+	+
W3092	Gal_2–	–	+	+	+
W3094	Gal_4–	+	–	+	+
W3096	Gal_6–	+	–	+	+
W3097	Gal_7–	+	–	+	+
W3178	Gal_8–	–	+	+	+
W3142	Gal–*	–	+	+	+

* No designation for this mutant, which is not linked in the same cluster as the others, has yet been published (*15*).

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Morse, E. M. Lederberg and J. Lederberg for the generous supply of *E. coli* mutants and for helpful discussions. I am also indebted to H. M. Kalckar for helpful suggestions made during the course of this work.

4. Abbreviations: ADP and ATP, adenosine di- and triphosphate, respectively; G-1-P, α-glucose-1-phosphate; Gal, D-galactose; Gal-1-P, α-galactose-1-phosphate; PP, inorganic pyrophosphate; UDPG, uridine diphosphoglucose; UDPGal, uridine diphosphogalactose; UTP, uridine triphosphate.
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14 November 1956

Studies on Metabolism of Carbon-14-Labeled Galactose in a Galactosemic Individual

It is frequently reported (*1*) that in congenital galactosemia only about 60 to 80 percent of the galactose administered can be accounted for on the basis of urinary excretion. The fate of the remaining galactose has, so far, been virtually unknown. However, Schwartz *et al.* (*2*) have recently demonstrated that galactose administration to galactosemic children brings about a significant accumulation of a hexose phosphate identified as galactose-1-phosphate. This poses the question whether the galactose retained in the body as galactose-1-phosphate might not account for the major part, if not the total, of the fraction of the galactose that is not excreted.

We have found (*3–5*) that in hemolysates, as well as in liver homogenates (*6*) from galactosemic subjects, the enzyme that catalyzes the metabolic step immediately succeeding galactose-1-phosphate formation (galactose-1-phosphate uridyl transferase) is defective or totally absent.

We were therefore interested in studying the galactose metabolism in man with special reference to: (i) galactose-1-phosphate accumulation and (ii) residual metabolism beyond the galactose-1-phosphate stage. Concerning the latter problem, it was felt that although enzyme studies reveal a defect of major proportion, a study of galactose metabolism in the intact human organism might detect the presence of appreciable metabolism beyond simple phosphorylation. Highly sensitive methods for detecting the conversion of galactose to the glucose of glucose derivatives were based on two principles: (i) The use of C^{14}-labeled galactose and (ii) the trapping of galactose as a glucosiduronic acid. The latter principle was used for several reasons.

Studies during the last few years have shown that the irreversible conversion of glucose to glucosiduronic acids involves the very same uridine nucleotides that are operating in the conversion of galactose to glucose derivatives (*7*). Moreover, the conversion of galactose and glucose compounds to alcohol glucosiduronic acids gives rise to compounds that can readily be isolated as crystalline precipitates.

Galactose-1-C^{14} (*8*) was administered intravenously over a period of 30 minutes to a 24-year-old male with galactosemia in a dose of 5 μc. In this experiment, 1 g of nonisotopic galactose was added to the galactose-1-C^{14} being infused. Concurrent with the administration of the isotope, the subject ingested 1 g of menthol over a period of 24 hours. Urine was collected at 2-hour intervals during this time. From each collection, menthyl glucosiduronic acid was isolated as the ammonium salt (*9*) and purified (*10*).

An aliquot of the urine was taken prior to isolation, acidified, extracted with redistilled ether, and total menthyl glucosiduronic acid was determined on the ether extract by the orcinol reaction using the conditions described by Dische (*11*). The purified menthyl glucosiduronic acid was counted in solution in a Packard Tri-Carb liquid scintillation spectrometer. A sample of the substrate galactose-1-C^{14} was counted in the same way.

From the radioactivity of the pure menthyl glucosiduronic acid and the quantity of the compound excreted, total counts were calculated. From this figure and the counts administered as galactose-1-C^{14}, the percentage conversion of the substrate to glucosiduronic acid was computed. Urea was isolated for the purpose of sampling the CO_2 pool. Urinary galactose was measured by the method of Nelson (*12*) as the reducing sugar remaining after treatment of the urine with glucose oxidase (*13*). Galactose and galactose-1-phosphate in blood were detected by indirect methods. No detectable counts were found in the blood plasma. However, in the erythrocytes, appreciable amounts of counts were found (see Table 1).

The presence of galactose-1-phosphate was inferred for the following three reasons. (i) The C^{14}-labeled material was confined to the erythrocytes, with no radioactive material present in the plasma fraction. Free galactose would be distributed fairly evenly between the two fractions. (ii) The reported observation of galactose-1-phosphate accumulation in the erythrocytes from congenital galactosemia has been reported (*2, 3*). (iii) Enzymatic assay, although it was too low to be considered quantitative, revealed traces of galactose-1-phosphate (*4*).

Excreted galactose and glucosiduronic acid were measured as described. The amount of suspected galactose-1-phosphate present in the relatively small blood specimens was too minute to isolate. The radioactivity measurements were therefore performed directly on small samples of crude filtrates, and corrections for self-absorption were made. Counts for a known sample of C^{14}-labeled galactose were taken under identical conditions—that is, as an internal standard. In this way counts could be expressed as micromoles of galactose.

Filtrates from plasma were found to be nonradioactive, whereas filtrates from erythrocytes showed distinct radioactivity. The latter could not be attributed to free galactose because galactose would distribute itself freely between plasma and cells. It was therefore classified as "cellular" galactose, for any cellular incorporation of radioactivity would figure on the balance as galactose retained in the body. This is actually the essential term in the balance. From the studies by Schwartz *et al.* (*2*) as well as those by us (*5*), it seems likely that all of the cellular galactose is identical with galactose-1-phosphate.

The distribution of galactose which was found over a period of 4 hours is shown in Table 1. As can be seen, out of the 1 g of galactose administered, 75 to 80 percent was not metabolized beyond the galactose-1-phosphate stage, 3 percent was metabolized to the glucosiduronic acid stage, and 20 to 25 percent was not accounted for. The latter fraction was probably metabolized to carbon dioxide or lactic acid but diluted by carbon from the general carbohydrate pool so as to escape detection, for the urea

Table 1. Balance of galactose compounds (after the infusion of 1 g of galactose and 5 μc of galactose-1-C^{14} to a 24-year-old male with galactosemia).

Item	Amount (mg)
Galactose excreted in urine	700
Galactose metabolized to glucosiduronic acid	30
Galactose accumulating as "cellular" galactose (galactose-1-phosphate and so forth)	50 to 100*

* All tissues with the exception of muscle and bone.

contained no C^{14}. A possible loss by excretion through the gastrointestinal tract cannot be excluded.

We believe that the galactose was not only metabolized to glucosiduronic acid but that most of the remaining 200 mg of galactose was generally metabolized. This belief is partly based on an experiment in which only 1.5 mg of galactose-1-C^{14} (undiluted) was administered. In the afore-mentioned experiment, it was established that the galactosemic organism is able to metabolize 30 mg of galactose to glucosiduronic acid. One would therefore expect that if the latter pathway were the only one in operation, a minute amount of galactose, such as the 1.5 mg of C^{14}-labeled galactose that was administered in a separate experiment, would readily be completely converted to glucosiduronic acid. However, the experiment showed that only 6.5 percent of this amount appeared as glucosiduronic acid. The most reasonable assumption is that the rest went through the pathway of glucose-6-phosphate and hence escaped detection by high isotope dilution. These considerations probably also apply for the experiment in which 1 g of galactose was administered.

The special value of the isolation and analysis of the C^{14}-labeled menthyl glucosiduronic acid is manifold. (i) It demonstrates directly that galactose can definitely be metabolized in the galactosemic organism. (ii) It poses a question as to whether the block of the galactose-1-phosphate uridyl transferase is complete, for it is known from earlier studies that conjugated glucuronic acid arises from hexoses through the uridine nucleotides (*7*).

That the normal pathway, or a very closely related accessory one (compare *14*), was in operation in this case is also supported by the fact that the distribution of labeled carbon in the glucuronic acid moiety was identical with that of the galactose administered—that is, it was confined to carbon atom 1 (*15*).

A normal adult person is able to metabolize 20 to 25 g of galactose within 12 hours (*16*), whereas a galactosemic person is able to metabolize 150 to 200 mg at the most. This means that a galactosemic subject has retained only about 1 percent of the capacity of a normal person with respect to galactose metabolism. This is a somewhat lower than, but probably in the order of magnitude as, that found *in vitro* by enzymatic assays on liver tissue obtained from the same patient (*6*). It was estimated that less than 4 to 8 percent of the normal activity of the galactose-1-phosphate uridyl transferase was retained in the galactosemic liver. Alternatively, the activity could be attributed to an incorporation enzyme related to galactose-1-phosphate uridyl transferase. The red cells from the same subject showed no detectable amounts of galactose-1-phosphate uridyl transferase.

The values obtained from *in vitro* and *in vivo* studies definitely fall into the same order of magnitude. The *in vivo* method is for this particular purpose as sensitive as the *in vitro* technique. Both methods may give the approximate residual galactose-1-phosphate uridyl transferase present in the galactosemic subject. However, it is quite naturally not possible to rule out the existence of a closely related accessory exchange mechanism involving galactose-1-phosphate, which is replacing the normal pathway in congenital galactosemia.

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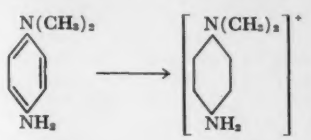
14 November 1956

Oxidation of N,N-Dimethyl-p-phenylenediamine by Serum from Patients with Mental Disease

In investigations carried out at the Långbro Mental Hospital in 1955, it was found that fresh blood serum obtained from patients with mental disease, including schizophrenic, manic depressive, and senile psychoses (*S*-serums) had the capacity to oxidize N,N-dimethyl-*p*-phenylenediamine (DPP) more rapidly than fresh serum obtained from healthy control subjects (*N*-serums). Further investigations to determine the incidence of this reaction in nonmental diseases and to explore the possibility of using it as a diagnostic test for mental disease are in progress. This report describes the biochemical background that underlies this reaction (*1*).

Mild oxidation of DPP leads to the formation of a free radical of a semiquinone type (see for example, *2*):



This substance has an absorption maximum at 552 mμ and is known as Wurster's red.

The addition of DPP (*3*) to fresh serum from healthy control subjects is followed by a lag period of approximately 5 minutes, during which there is but slight increase in the extinction at 552 mμ. A sudden acceleration in color development then ensues, with a linear increase in extinction. In contrast, the lag period in development of the red color is much shorter or absent with fresh *S*-serum (Fig. 1).

Prolonged exposure to room air, gentle aeration, or dialysis against 0.9-percent NaCl increases the capacity of *N*-serum to oxidize DPP so that it equals or approaches the rate characteristic of *S*-serum. This suggests that one or several reducing substances of low molecular weight which are present in *N*-serum are quantitatively diminished or absent from *S*-serum.

The DPP-oxidizing substance in both serums is heat labile and not dialyzable. It therefore appears to be a catalytically active protein.

The ability to oxidize DPP disappears when serum is dialyzed against a citrate-phosphate buffer of *p*H 3. Following removal of buffer ions by dialysis against 0.9-percent NaCl, this activity can be restored by addition of a low concentration of Cu^{++} ions but not by Fe^{+++} ions. This finding suggested that ceruloplasmin, a serum oxidase containing copper, which was first isolated by Holmberg and Laurell (*4*), might be involved. Ceruloplasmin constitutes the copper-binding protein of normal serum. It contains about 95 percent of the total serum copper (*5*) and is also capable of catalyzing the oxidation of *p*-phenylenediamine.

Evidence suggesting that catalytic oxidation of DPP by serum is attributable to ceruloplasmin was provided by finding that this activity is precipitated with $(NH_4)_2SO_4$ in the same fraction as is ceruloplasmin. Furthermore, DPP oxi-

dation by serum resembles ceruloplasmin activity in that it is strongly inhibited by NaN_3 but not by NaF, NH_4-oxalate, or cystine (inhibitor concentration about 1 mg/ml). A concentration of $2 \times 10^{-4}M$ NaN_3 produced 67-percent inhibition of serum DPP oxidase activity at *p*H 6.6, a value similar to that reported for pure ceruloplasmin with *p*-phenylenediamine as substrate (*6*). Other enzyme inhibitors such as Na-diethyldithiocarbamate, KCN, and cysteine could not be tested by this method because they decolorize DPP_{ox}.

Finally, addition of ceruloplasmin (*7*) to serum showed that DPP actually is a substrate for this enzyme. Thus the catalytically active protein responsible for DPP oxidation by serum is probably identical with ceruloplasmin.

Elevated serum copper levels have been found in schizophrenia (*8*), and recently Ozek (*9*) has shown that this increase in serum copper is attributable to an abnormally high ceruloplasmin content. Confirmation of elevated ceruloplasmin activities in *S*-serums has been obtained using DPP as substrate.

As has already been pointed out, the reducing substance (or substances) predominantly present in fresh *N*-serum is rapidly autooxidized and is dialyzable. The addition of organic Hg-halides or N-ethyl-maleiimide to *N*-serum does not effect the capacity of the serum-reducing substances to decolorize DPP_{ox}. However, the addition of physiological amounts of ascorbic acid to dialyzed *N*-serum restored its capacity to reduce DPP_{ox} (Fig. 2). It thus appears that ascorbic acid, which is present in serum in amounts of about 1 to 25 μg/ml, is responsible for at least a part of the reducing capacity of serum. It is further known that the serum ascorbic acid content is low in schizophrenia (10).

To determine whether ascorbic acid is the sole or the predominant reducing substance in serum, the effect of the addition of various amounts of ascorbic acid

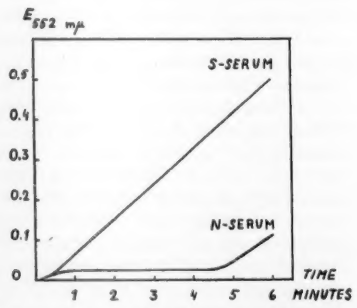


Fig. 1. Typical oxidation curves for DPP in serum; *S*-serum was from an acute schizophrenic; *N*-serum was from a healthy person; 1.5 ml of serum and 1.5 ml of 0.1-percent DPP · 2HCl in distilled water; the blank contained 1.5 ml of serum and 1.5 ml of distilled water.

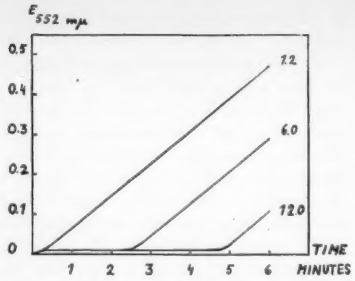


Fig. 2. Addition of ascorbic acid to dialyzed serum; 1.4 ml of dialized serum, x ml of ascorbic acid stabilized in albumin solution, $(0.1 - x)$ ml of distilled water, and 1.5 ml of 0.1-percent DPP · 2HCl in distilled water. The figures on the graph denote the added ascorbic acid (x) in micrograms per milliliter.

to dialyzed serum was investigated. Figure 2 shows that the time T during which DPP is maintained in the reduced state, as indicated by the failure of the extinction at 552 mμ to increase, is lengthened by increasing the concentration of ascorbic acid. In each instance, T is approximately proportional to the ascorbic acid content.

However, in addition to the effect of ascorbic acid, it is to be expected that T would vary inversely with the DPP oxidase activity of individual serums. The ceruloplasmin activity is indicated by the slope v of the curves in Figs. 1 and 2. If ascorbic acid is the only reducing substance playing an effective role in this reaction, a quantitative estimate of its concentration in serum can be obtained by calculation from the ceruloplasmin activity as indicated by the slope v and the measured T-value according to the following equation:

$$[\text{Ascorbic acid}] = kvT \qquad (1)$$

where k is a constant.

Variable amounts of ascorbic acid were added to a number of dialyzed serums having different ceruloplasmin acitivties, and T and v were measured. Equation 1 was found to be valid, and a k-value of 30 was found at $21 \pm 2°C$ (*11*).

It is pertinent to discuss the role of physically dissolved oxygen in this reaction and whether it is present in sufficient amounts to support the oxidation of DPP during the period of the test—that is, 5 to 6 minutes. From Eq. 1 it follows that the rate of oxidation of ascorbic acid in *N*-serum ($v \approx 0.08$) is about 2.4 μg/min (1.4×10^{-2} μmole/min), which is equivalent to 2.8×10^{-2} μmoles of DPP per minute, since 1 mole of ascorbic acid reduces 2 moles of DPP_{ox}. The concentration of dissolved oxygen in venous serum (plasma) is about $60\mu M$. In the test, 1.5 ml of serum is used, thus containing about 9×10^{-2} μmoles of O_2. It is thus apparent that the physically dissolved oxygen in serum is sufficient to account for the oxidation of DPP for about 13 minutes at the aforementioned rate, since each mole of O_2 is capable of oxidizing 4 moles of DPP. Actually, the capacity of the reaction mixture to oxidize DPP is greater, because the distilled water used contains an appreciable amount of dissolved O_2.

The ascorbic acid concentrations calculated by measuring T and v and inserting the values in Eq. 1 were compared with the ascorbic acid concentrations found by chemical analysis (*12*) of 16 different serums from both mentally diseased and healthy subjects. Good agreement between the calculated and measured values was obtained in all cases investigated, and it appears that ascorbic acid accounts for at least 95 percent of the substance in serum that is capable of reducing DPP_{ox}.

This method affords a simple means for determining the approximate concentration of ascorbic acid in serum, which should be adequate for most clinical purposes. The error is about ± 1 μg ascorbic acid per milliliter of serum. However, T is short and more difficult to measure when the ascorbic acid concentration is very low.

In those serums investigated, the ceruloplasmin activity was usually proportional to the copper content. However, rather large deviations were sometimes observed, probably depending on protein —SH— groups present in varying concentrations in different serums. These were shown to inhibit the ceruloplasmin activity, because the inhibition could be prevented by the addition of organic Hg-halides to serum.

It may be concluded from these studies that the difference between *N*-serum and *S*-serum in their capacities to oxidize DPP is dependent mainly on the fact that the ceruloplasmin activity is higher and the ascorbic acid concentration lower in *S*-serum than in *N*-serum.

The possibility of using this color reaction as a diagnostic test in mental disease is now being investigated. However, it cannot be regarded as specific for mental disease, since there are other conditions in which serum ascorbic acid concentration may be lower and serum ceruloplasmin activity higher than normal (for example, liver disease, pregnancy).

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1. My sincere thanks are due to Hugo Theorell for his kind interest in this work and for the hospitality of his laboratory, to Erik Goldkuhl for suggesting this field of investigation and for supplying serums, and to George Ludwig for aiding with the manuscript. This work was supported by a grant from the Swedish Medical Research Council.

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17 December 1956

Penicillin-Induced Lysis of Escherichia coli

This communication reports some results of studies the objective of which was the elucidation of the mechanism of the bactericidal action of penicillin. Those of our findings which are coincidental to the observations of Liebermeister and Kellenberger (*1*) and of Lederberg (*2*) on the penicillin-induced emergence of bacterial protoplasts were established independently.

While several metabolic processes in microorganisms are known to be influenced by penicillin, none of them has been shown conclusively to be the site of the primary action of the antibiotic, and thus, to be originally responsible for the antibacterial action of the drug (*3*). The present report is concerned with the lysis of *Escherichia coli* induced by penicillin, a phenomenon that points to profound disturbances of cell-wall functions.

Escherichia coli strain B was used as the test organism (*4*). The method for spectrophotometric assay of antibiotic action has been described elsewhere (*5*). Figure 1 shows the lysis of *E. coli* B under the influence of 100 units of penicillin per milliliter; the rates of lysis were approximately dependent on penicillin concentrations over a range from 12.5 to 500 units/ml.

Penicillin-induced lysis of *E. coli* occurred only in a nutritional environment that was capable of supporting the growth of the bacteria. Logarithmic cultures of *E. coli* which were washed free of growth medium and then resuspended in fresh media devoid of sources of carbon or nitrogen did not undergo lysis in the presence of penicillin, while bacteria that were resuspended in complete growth medium lysed as usual.

When 100 units of penicillin per milliliter was added to logarithmic mass cultures of *E. coli* B and vigorous aeration was continued, the cultures soon began to foam, and masses of macroscopic, long strands that gave the impression of highly polymerized material appeared. Strands collected by low-speed centrifugation were readily dissolved in 0.5N NaOH to form viscous solutions, while some residue remained when the strands were extracted with 5 percent perchloric acid for 30 minutes at 70°C. The ultraviolet absorption spectra of such perchloric acid extracts closely resembled those of nucleic acids. Chemical analysis indicated that about 15 percent of the total nitrogen of the strands went into the perchloric acid extracts. These extracts also contained quantities of pentose and deoxypentose, which suggested the presence of ribonucleic and deoxyribonucleic acids in a ratio of 3.5 to 1.

Another method of lysing bacteria, depolymerization of the cell walls by lysozyme, exposes the bacterial protoplasts (*6*), which, in an unfavorable osmotic environment, are disrupted and yield the cytoplasmic constituents in an alkali-soluble form that contains highly polymerized deoxyribonucleic acid (*7*).

In order to investigate the possibility that protoplasts might become demonstrable also as the result of penicillin action, sucrose was added to logarithmic cultures of *E. coli* B to give molar concentrations of 0.32 or 0.48. Penicillin, to a concentration of 50 units/ml, was added 30 minutes later. Incubation was continued without aeration or mechanical agitation, and samples were taken at 30-minute intervals for spectrophotometric readings and examination under the phase-contrast microscope. Figure 1 shows the time course of penicillin action in the presence of 0.32M and 0.48M sucrose.

Observation under the phase-contrast microscope (Fig. 2) revealed the following sequence of events: the bacterial rods produced central or terminal globular extrusions that increased in size while the bacterial cell walls became correspondingly empty of cytoplasm. Later, the globes either separated from the cell walls or retained parts of them attached,

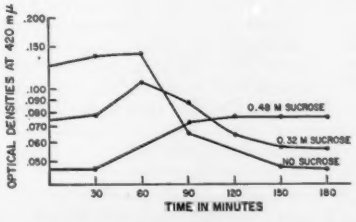

Fig. 1. Lysis of *E. coli* B by 100 units of penicillin per milliliter in the absence and presence of sucrose.

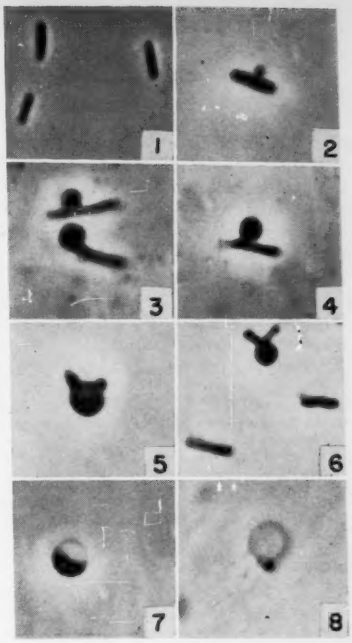

Fig. 2. Sequential phases of penicillin-induced lysis of *E. coli* B: 1, Bacteria immediately after addition of penicillin; 2, 3, and 4, emergence of globular extrusions; 5 and 6, "rabbit ear" forms; 7, partially vacuolized globular structure; 8, "ghost" form of a cytoplasmic membrane.

giving a typical "rabbit-ear" appearance. Finally, the globular structures underwent partial vacuolization, showing many crescent-shaped forms; eventually they released their entire content, leaving as formed elements only circular "ghosts" that probably represented empty cytoplasmic membranes.

The emergence from bacteria of spherical structures, called "large bodies," has been the subject of a literature more extensive than conclusive. The present morphological observations resemble those of Liebermeister and Kellenberger (*1*) concerning the action of penicillin on *Proteus vulgaris* in liquid cultures; these two authors also have emphasized the similarity between "large bodies" and bacterial protoplasts. For *E. coli*, this idea has been further expanded by Lederberg (*2*).

The present findings on the lysis of *E. coli* by penicillin are consistent with the following interpretation: the drug induces a metabolic change that affects the integrity of the bacterial cell walls in such a way that the content of the bacteria, enclosed in a cytoplasmic membrane, extrudes as a globular structure. Without protection against osmotic and mechanical disruption, the globes disintegrate and release the cytoplasmic material. In the presence of appropriate

concentrations of sucrose, on the other hand, the disruption of the globes is sufficiently retarded to permit the demonstration of the sequential phases of the lysis.

An elucidation of the primary action of penicillin on bacterial cell walls may well provide one of the clues to the mechanism of action of the drug. Park and Strominger (*8*) have provided a definitive chemical basis for an explanation of the primary action of penicillin.

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31 October 1956

Effect of Digoxin on Myokinase Activity

In a study of "energetic-dynamic cardiac insufficiency," Munchinger (*1*) reported that strophanthin and digilanid enhanced the adenosine triphosphatase (ATPase) activity of rat-heart homogenate. Attempts to repeat this observation using actomyosin prepared from heart gave results that varied from 40 percent to zero activation, depending on the relative purity (by reprecipitation) of the actomyosin preparation. The loss of digoxin enhancement on reprecipitation indicated that a component other than actomyosin was sensitive to digoxin. The present report suggests that this component may be myokinase (*2*).

Actomyosin (myosin B) was prepared from dog heart by the method of Szent-Gyorgi (*3*). Adenosine triphosphatase activity was measured by incubating myosin B and adenosine triphosphate (ATP) in KCl (0.15*M*)- veronal buffer (0.02*M*) at *p*H 7.3 At the end of the incubation time, 20-percent trichloroacetic acid was added, the mixture was centrifuged, and phosphorus was determined on an aliquot of the supernatant by the method of Fiske and Subbarow (*4*).

Myokinase was prepared according to Kalckar's method (*5*). The final trichloroacetic acid precipitation was omitted. The myokinase solution was dialyzed against distilled water and finally centrifuged at 18,000 *g* for 30 minutes. The final product contained 0.28 mg of N per milliliter and showed only one major peak when subjected to electrophoresis for 90 minutes in 0.1*M* veronal buffer at *p*H 8.5.

Myokinase activity was determined following the procedure of Bendall (*6*). A myosin B preparation was used as a specific ATPase hydrolyzing only the terminal phosphate group of ATP. Because the myosin B was in sufficient excess to hydrolyze 45 to 46 percent of the 10-minute acid-labile phosphate of ATP in 2 minutes, the extra phosphate liberated in 10 minutes was a function of the myokinase concentration and was taken as myokinase activity. The myokinase preparations, when present in optimum concentration, liberated 100 percent of the 10-minute labile phosphate.

We found that myosin B from rat heart was difficult to free from myokinase activity, whereas that from dog heart was relatively easy to free. Myosin B from dog heart was therefore chosen for the test system. Figure 1 shows the effect of digoxin on myokinase activity. The myosin B and ATP concentrations are constant throughout. Bars 1 through 6 denote increasing quantities of myokinase added to the test system. The activating effect of digoxin appears to be confined to the systems in which myokinase is a limiting factor. At high myokinase concentrations (bar 6), the total activity was inhibited, and digoxin had no influence on the reaction. This decrease of the over-all reaction was apparently the result of inhibition of ATPase activity of

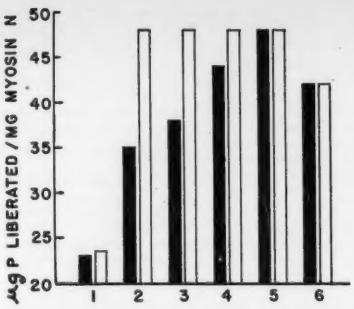

Fig. 1. Effect of digoxin on the activity of myokinase. The incubation tubes contained the following: KCl, 0.15*M*; veronal buffer, 0.02*M* at *p*H 7.3; $CaCl_2$, 0.01*M*; ATP, $3.75 \times 10^{-4}M$, myosin B (0.46 mg N/ml, 0.2 ml; and digoxin, 10 μg/ml. The total volume was 2.0 ml. Black bars, controls; open bars, with digoxin. Myokinase (0.28 mg N/ml) was added as follows: bar 1, none; bar 2, 0.025 ml; bar 3, 0.05 ml; bar 4, 0.1 ml; bar 5, 0.2 ml; bar 6, 0.5 ml.

myosin B rather than to an effect on myokinase activity. At a lower myokinase concentration (bar 5), which appears to be the optimum myokinase concentration in our test system, digoxin was without effect. When the myokinase concentration was decreased below the optimum level (bars 2, 3, and 4), digoxin activated the myokinase reaction, bringing the reaction to the level obtained with optimum concentrations. With no added myokinase, digoxin had no effect on the ATPase activity of myosin B.

Hasselbach and Weber (*7*) have shown that the Marsh (*8*) and Bendall (*9*) relaxing factor of muscle inhibits the ATPase activity of myosin by extending substrate inhibition to physiological concentrations. The demonstration of Bendall (*6*) that the Marsh-Bendall factor exhibited all the characteristics of myokinase prompted us to include in the present study the effect of digoxin on the ATPase-inhibiting characteristics of myokinase. Table 1 shows the effect of digoxin on the myokinase inhibition of ATPase activity of myosin B at two concentrations of ATP. At lower ATP concentrations (0.005*M*), the myokinase inhibition is slight (32 percent) but the ability of digoxin to reverse myokinase inhibition is evident. At higher ATP concentrations (0.01*M*), inhibition approaches 73 to 74 percent, and the ability of digoxin to reverse the myokinase effect is obvious.

According to Weber (*10*), contraction of muscle is associated with ATP breakdown and lasts as long as ATP continues to be hydrolyzed. Relaxation sets in as soon as ATP breakdown is prevented. Physiologically induced relaxation is based on an inhibition of ATP hydrolysis by the Marsh-Bendall factor (myokin-

Table 1. Effect of digoxin on the myokinase inhibition of ATPase activity of myosin B at two concentrations of ATP. The figures are based on 6 individual runs. Three runs were made on one myosin and myokinase preparation and three runs were made on a different myosin and myokinase preparation. The tubes contained the following: KCl, 0.15*M*; veronal buffer, 0.02*M* at *p*H 7.3; $MgCl_2$, 0.005*M*; myosin B (0.46 mg N/ml), 0.15 ml; myokinase (0.28 mg N/ml), 0.5 ml; and digoxin, 10 μg/ml. The total volume was 2.0 ml.

ATP Concn. (*M*)	Phosphorus liberated (μg/mg of myosin N hr)			
	Control	Digoxin	Myokinase	Myokinase and digoxin
0.005	1842 ± 24	1868 ± 28	1270 ± 36	1884 ± 32
0.01	1520 ± 58	1610 ± 32	402 ± 27	1458 ± 60

ase). It would appear that activity within the area of myokinase might allow digoxin to enhance the contractile response of muscle at the expense of relaxation by (i) activating the myokinase reaction (ADP → ATP) and (ii) by suppressing myokinase inhibition of myosin ATPase.

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6 December 1956

Spectral Reflectance Applied to the Study of Heme Pigments

It is a common practice to make qualitative and rough quantitative estimates of the content of pigmented substances in materials by the intensity and spectral distribution of color. It is rather surprising, then, that more use has not been made of spectral reflectance in qualitative and quantitative analytic chemistry. It is the intention of this report (*1*) to point out the potentialities of the method, particularly in biochemical analysis, and to illustrate its application in the investigation of certain heme pigments.

The use of spectral reflectance curves in the specification of color by the physicist is well known. Lermond and Rogers (*2*) have recently pointed out the possible wider utility of spectral reflectance measurements in chemical analysis and have reviewed the limited amount of work in this field. Applications in biochemistry seem to be particularly rare.

In the course of research on pigment systems in fish flesh, we investigated the use of spectral reflection measurements. A standard reflection attachment to the Beckman DU spectrophotometer was used. Samples, either 90-mesh, nonabsorbing powders with absorbing solutions or solids added, or tissue forced through a 16-mesh, stainless-steel screen, were packed into 1¼ by 1/16-in. aluminum planchets and covered with glass plates. Comparison was made with a standard consisting of the nonabsorbing diluent powder or with a disk of high-fired alumina.

Adherence to Beer's law was tested by adding different amounts of standard copper sulfate solution to the crystalline alumina diluent and measuring the absorbancy at 620-mμ wavelength. The law seems to be applicable at this wavelength and for the range of concentrations indicated (Fig. 1). These results are at variance with those that Winslow and Liebhafsky (*3*) reported for reflectance from known concentrations of metals spot-tested on paper. The discrepancy may be due to the difference in the thickness of the supporting media for the samples used in the two experimental situations. Measurements were attempted with whole blood dispersed on 90-mesh crystalline alumina. In this case, adherence to Beer's law was found at low concentrations, but oxidative changes caused deviation in the higher range.

In transparent, internally absorbing systems (dielectrics), it can be assumed that reflection takes place at phase interfaces and by diffuse scattering from large molecules. Adherence to Beer's law would signify that, for systems of similar opacity, the average path length of the incident and emergent beam is the same and would also justify the use of absorbancy (optical density) in the plotting of spectral reflectance data. Thus spectral reflectance can presumably be used for the comparative quantitative analysis of stable systems of dielectric materials of similar general composition. Such measurements have been applied in the present work.

The use of the method for the characterization of pigments by their reflectance curves is illustrated in Fig. 2. Various derivatives of respiratory pigments can be identified in the reflection spectra of tuna flesh that is exposed to a variety of oxidative environments. An advantage afforded by this technique is the possibility of evaluating the spectral absorbance of opaque concentrated systems without recourse to the special cells, or to dilution in solution with its attendant possibility of alterations, that are employed in transmission methods. For example, the spectrum of whole human blood can be directly determined using an inert crystalline alumina diluent (Fig. 2*c*).

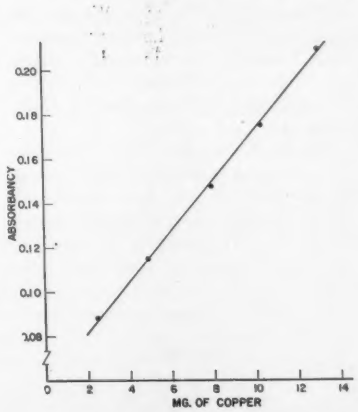

Fig. 1. Beer's law plot for copper on 90-mesh crystalline alumina.

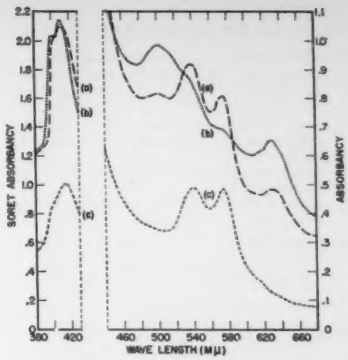

Fig. 2. Spectral reflectance curves *a*, mixed oxymyoglobin and metmyoglobin in tuna flesh; *b*, metmyoglobin in tuna flesh; *c*, oxyhemoglobin in whole blood.

Spectral reflectance is particularly suited to *in situ* studies on pigment systems where extractive procedures are difficult or impossible or where such procedures would cause undesirable changes. It is characteristically a simple technique in that a minimum of preparative and extractive operations is involved. Specifically, absorbance studies on coagulated proteins were possible; in addition, the examination of residues after the extraction of certain components gave a more complete picture of extraction efficiency and relative solubilities. Furthermore, one is able to follow the course of induced or natural chemical reactions in such systems. For the heme protein systems studied, the wavelengths of absorption maxima in reflection corresponded exactly to those found in transmission, and complete interchangeability of data was noted. Thus the large amount of data accrued from measurements in transmission would be available to workers in the field of reflectance in systems where this interrelationship is found to be true.

The measurement of spectral reflectance offers a method for the study of dielectric materials that absorb and reflect internally, as opposed to surface reflectors such as metals. It is felt that this investigative tool merits the further attention of the biological and analytic worker.

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References and Notes

1. This work was supported by contract No. 14-19-008-2475 with the Pacific Oceanic Fishery Investigations (POFI), U.S. Fish and Wildlife Service. We wish to express our appreciation to A. L. Tester and other members of the staff of POFI, and to F. Jermann of Hawaiian Tuna Packers, for aid in this work.
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25 October 1956

Reactions of Honey Bees in the Hive to Simple Sounds

Beekeepers have known since before Aristotle (*1*) that honey bees (*Apis mellifera*) produce characteristic sounds while engaged in certain activities. The possible significance of these sounds for the bees has been a matter of debate (*2, 3*). Indeed, honey bees seem to be insensitive to air-borne sounds, although they are able to receive vibrations through the legs (*3, 4*). Hansson (*3*) has reported that bees in hives stopped normal activities when they were subjected to pure tones at frequencies of 100 to 1500 cy/sec at rather high intensities (audible at distances up to 250 m). The insects stopped moving when the sounds were turned on, but, if the sounds continued, began to move slowly within a few seconds.

We have confirmed and extended these observations by finding that continuous irradiation of hives with sounds of certain frequencies and of sufficient intensities caused an almost total cessation of movement of workers and drones in the hives for up to 20 minutes (*5*). The quiescence of the bees was so complete that a beekeeper could safely open the hive and carry out routine servicing without the usual treatment with smoke.

Sounds of known frequencies were produced by an audio oscillator that activated through an amplifier either a loudspeaker (for frequencies below 400 cy/sec) or a microphone (for higher frequencies) (*6*). The behavior of the honey bees, all of the Italian race, was observed in an ordinary glass-sided observation hive. The speakers were usually placed about 0.5 to 1 m from the hive, but tests were also made with the speakers in contact with the hive. The results are given in Table 1.

Table 1. Effects of sounds on honey bees in an observation hive: 0, no observable effects; +, bees move more slowly; ++, the majority of the bees stop but some still move slowly; +++, almost all bees stop and remain motionless as long as the sound is on. The sound pressure for frequencies with +++ effect are minima needed to induce the effect; other sound pressures are the highest obtainable with the equipment.

Frequency (cy/sec)	Sound pressure (db)	Effect
50	106	0
80	115	0
100	120	+
150	125	++
200	122	++
300	119	+++
400	118	+++
500	116	+++
600	107	+++
800	108	+++
1000	113	+++
1500	124	++
2000	128	+
3000	127	0
4000	117	0
6000	112	0
8000	113	0
10000	102	0

With sounds of sufficient intensity at frequencies of 300 to 1000 cy/sec, the bees stopped moving almost entirely as long as the sounds continued. The most effective frequencies were between 500 and 800 cy/sec. Below 300 and above 1000 cy/sec, the bees either showed reduced activity or were not affected, even with intensities higher than those that sufficed at the proper frequencies. The bees returned almost immediately to normal activities when the sound was discontinued. There were no observable reactions to these sounds by bees at the entrance to the hive or by workers in the field. These observations support the idea that the sounds are received by the bees through the legs after the hive was caused to vibrate by absorption of the air-borne sound. The most effective frequencies in this case, however, were not those found by Autrum and Schneider (*4*) to be most effective in stimulating the subgenual organs in the legs of the honey bee.

The results are like those of Hansson (*3*), except that cessation of activity at the intensities we used was almost complete and persisted as long as the sound continued. It is impossible to determine from Hansson's report the actual intensities he used, but they were probably lower than those we used.

Bees in standard beehives were tested with similar results. With the sounds on, the covers and supers of the hives were removed and the frames lifted out. The bees on the frames remained still as long as sounds of the proper frequencies and intensities continued. It was possible, therefore, to work in hives using only sound. This was done for about 2 months with three hives, using sound at a frequency of 600 cy/sec at about 120 db, which was projected from a speaker alongside the hive. There was no sign of habituation of bees to this sound.

Certainly the equipment used to produce these sounds is much more expensive than that needed for smoking hives. It is possible, however, that inexpensive vibrators attached to hives could be used. The high intensities of these sounds make some form of ear protection necessary, but free use of both hands in working in the hive is possible and there is no need for ventilation of the hive by the bees, as there is with smoke. Sound may thus, under special circumstances, have some use in apiculture.

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6. Hewlett-Packard audio oscillator model 200-A; Stromberg-Carlson amplifier model AU42; University loud speaker model PA-30; Altec microphone model 633A. Sound pressures in decibels re 10^{-16} watt/cm^2 were measured at 1 m from the speakers with a calibrated Scott sound-level meter type 410-B.

29 November 1956

Book Reviews

Man's Role in Changing the Face of the Earth. William L. Thomas, Jr., Ed. University of Chicago Press, Chicago, Ill., 1956. 1193 pp. Illus. $12.50.

This weighty volume (actually 5 pounds 9 ounces) contains the background papers for, and summaries of, the discussions which took place in June 1955 at Princeton, N.J., during an international symposium made possible by funds from the Wenner-Gren Foundation for Anthropological Research, Inc., the printing of the proceedings being aided by a grant from the National Science Foundation of the United States of America.

It is dedicated to George Perkins Marsh (1801–82), American statesman and scholar who in 1864 wrote of the need for caution in large-scale operations which modify the surface of the earth and suggested the importance of improvement of waste and exhausted regions (*Man and Nature*; or, *Physical Geography as Modified by Human Action*).

The symposium met at two sessions each of 6 days and was organized to consider, first, man's tenure of the earth, the subsistence economies, commercial economies, and the industrial revolution with the developing urban dominance; then, environmental changes through forces independent of man, man's effects on the waters of the earth, alteration of climatic elements, changes in soils through human use, modifications of biotic communities, ecology of wastes, and urban-industrial demands on land; followed by limits, as to materials and ideas, man's self-transformation, and the unstable equilibrium of man in nature; ending with a session for summary remarks by the three collaboration editors.

The magnitude and range of the work may be judged from the fact that 53 authors contributed background papers and 70 took part in the symposium. These were selected as thinking individuals from some 24 disciplines and ten countries.

A short review of such a wide-ranging work cannot do justice to any part of it, but reference may be made to a few selected points which leap to the eye. Only about ten generations separate us from the beginning of the scientific revolution, but in this short space of time man has wrought such changes and has engendered such conditions that they challenge his continued existence. The so-called "Western world" is made up almost wholly of urbanized individuals who regard natural resources as exploitative and expendable in an era of "expanding prosperity," with little or no thought for responsibility in the rapidly closing frontiers of the world. It was recalled that Putnam, in his *Future of Energy* said that half of the coal which has been burned in the whole history of the world has been burned in the United States in the last 30 years. Undoubtedly fossil fuels, after this century, will cease to exist in a practical sense.

It was a good thing to have some members of older civilizations from maybe so-called "underdeveloped countries" take part in the symposium to provide a balance to some of the more mechanical, technologic ideas prevalent in our own lands. Naturally there is some variation in the quality of the papers, but the general standard is high, and the volume as a whole is so full of up-to-date and thought-provoking material that it will be an essential reference in every institution of learning.

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Engineering as a Career. Ralph J. Smith. McGraw-Hill, New York, 1956. 365 pp. Illus. $4.75.

This book, designed to serve as a guide for a two-unit orientation course of approximately 32 meetings for freshmen engineering students, is organized in three parts: "The engineering profession," "College training of the engineer," and "The engineering sciences." It is also suitable for a three-unit course in which more emphasis is placed on problems, many of which are listed in nearly every chapter. For a one-unit course the author suggests minimizing or omitting the treatment of the engineering sciences.

It is my hope that no orientation course based on this book will completely omit the four chapters in this section, which give the student previews of engineering materials and mechanics, steam power, internal combustion engines and refrigeration, electric circuits and machines, electronics, and engineering economy. This material should be very helpful in alleviating the common complaint of engineering freshmen that they "are not getting any engineering."

In the first five chapters of part one Ralph Smith develops and discusses definitions of *engineering* and *engineer* and gives an excellent brief history of engineering, a thoughtful discussion of engineering as a *profession*, and well-written descriptions of the major fields of engineering.

There follows a chapter, which is believed to be unique among orientation textbooks, devoted to a discussion of the *functions* of engineering. The author points out that, while *fields* of engineering (civil, electrical, chemical, and so forth) appeal to the engineer's *interests*, the *functions* of engineering (research, design, production, and so forth) are more closely related to his *aptitudes* and, hence, are "more meaningful from the standpoint of career planning." He then lists "in order of decreasing scientific emphasis" the major engineering functions of research, development, design, construction, production, operation and maintenance, application and sales, industrial, and management. He cautions that in industry various combinations of these functions are frequently found in the same department, or even in the same person. He then defines each function, discusses it in detail with illustrative examples, and lists desirable personal qualifications and type of training.

Included is a discussion of the "engineering spectrum," with a diagram indicating the relative extent to which each major function depends on each of the four major factors involved in engineering—namely, ideas (abstract scientific concepts and principles), things (machines, materials, structures, circuits), men (employees, associates, superiors, customers), and money (financing, costs, prices, profits).

This chapter should prove highly valuable to anyone who is responsible for the guidance of engineering students, but it seems regrettable that no mention is made of engineering teaching, a field of great and growing importance.

Also worthy of special mention are Chapter 7, which discusses the relative roles of the scientist, the engineer, and the technician as members of "the technical team," and Chapter 15 on the engineering method of problem solution. This chapter could well be used much earlier in the course than is indicated by its position in the book, especially if much use is to be made of problems.

The chapters on the economic status of

the engineer and the cost and value of a college education are provocative, although the teacher using the book as a textbook will do well to check the data presented, which change quite rapidly. Other stimulating chapters are those on "Oral and written reports," "Engineering drawings and graphs," and "Numbers, symbols, and mathematical tools."

On the whole this book, while it might be improved by certain rearrangements of material, is a valuable addition to the growing literature on the orientation of prospective engineers.

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The American Experiences of Swedish Students. Retrospect and aftermath. Franklin D. Scott. University of Minnesota Press, Minneapolis, 1956. 129 pp. $3.

Every year more than 30,000 foreign students come to the United States to spend some time in American institutions of higher education. The Social Science Research Council has launched a research program "that might lead to better understanding of the complex processes involved in cross-cultural education." The study reported in this book is part of this SSRC program. Franklin Scott has visited Sweden studying Swedes who have visited the United States.

Scott is an alert and sympathetic observer of Americans and Swedes, and his book is full of insights. One is a little disappointed, however, that the author has not utilized social-science methods more efficiently so as to bring his insights beyond the impressionistic stage. It is surprising to hear a social scientist say that "the study trip abroad is essentially an individual phenomenon which defies classification" and that "the simplest way to present the results would be through a series of biographical analyses." This would be to reject the challenge of science.

Fortunately, the reader is *not* presented with a series of unrelated case histories. Despite the quoted declaration, Scott does indeed set out to generalize as best he can, on the basis of impressions gained from extensive interviewing and reading.

Thus the Swedes are reported to be annoyed at the American university system, which does not allow the students the same degree of independence as do Swedish universities. (But even so, Swedish educational reforms are much influenced by American practices.) The Swedes are also indignantly commenting upon sex relations in America, which they characterize as "prime example of American immorality and hypocrisy"; while Sweden "emphasizes the inevitability and naturalness of sex."

Comparing interpersonal relations more generally, the United States comes out best: "The Swedes . . . are accustomed to a frigid correctness of manners; the cheerfulness and easy friendliness of Americans show them a new way of meeting people, and make a universal appeal." Visiting Swedes are also impressed by American ability to work in groups; the following example illustrates the point almost too well: "In one Swedish community two research institutions exist almost side by side: one is dominated by an academic dictator and rent by bitterness; the other is led in cooperative spirit by a scholar who had participative experience in two of the best American research institutes, and its atmosphere is happy, its work effective."

These illustrations will have to suffice to indicate the flavor of the report. Although this may not be social science at its most advanced stage, it is interesting and suggestive reading.

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Engineering Mathematics. Kenneth S. Miller. Rinehart, New York, 1956. 417 pp. Illus. $6.50.

In this book the author has not tried to be encyclopedic but has made a coherent and useful selection from the possible topics. Apparently intended mainly for electrical engineers, the book meets the current standards of mathematical rigor for courses with a similar title at the junior, senior, and graduate levels. Thus, heuristic arguments are emphasized, and physical applications are often used to guide the mathematics. Certain mathematical niceties are included in the appendices. The major portion of the book is concerned with methods for the solution of linear ordinary and partial differential equations. The chapters on networks and random functions will doubtless be attractive features when the major emphasis in such a course is on linear equations. The book seems to be a sound and teachable treatment.

The chapter titles and comment thereon are as follows: "Determinants and matrices"; "Integrals. Introduction of special functions"; "Linear differential equations. Includes Green's function and series solutions"; "Fourier series and integrals"; "Laplace transform"; "Network theory"; and "Random functions."

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New Books

Advances in Cancer Research. vol. 4. Jesse P. Greenstein and Alexander Haddow. Academic Press, New York, 1956. 416 pp. $10.

Metallurgy and Fuels. Series V, *Progress in Nuclear Energy.* H. M. Finniston and J. P. Howe. McGraw-Hill, New York; Pergamon, London, 1956. 805 pp. $21.

A World Geography of Forest Resources. Edited for the American Geographical Society by Stephen Haden-Guest, John K. Wright, Eileen M. Teclaff. Ronald Press, New York, 1956. 736 pp. $12.50.

The Liassic Therapsid Oligokyphus. Walter G. Kuhne. British Museum (Natural History), London, 1956. 149 pp. £4.

The Great Chain of Life. Joseph W. Krutch. Houghton Mifflin, Boston, 1957. 227 pp. $3.75.

Natural History of Birds. A guide to ornithology. Leonard W. Wing. Ronald Press, New York, 1956. 539 pp. $6.75.

Heredity and Your Life. An account of everyday human inheritance. A. M. Winchester. Vantage Press, New York, 1956. 333 pp. $5.

Pharmacognosy. Edward P. Claus, Ed. Lea & Febiger, Philadelphia, ed. 3, 1956. 731 pp. $12.50.

Intercrossing among Pink Calla, White-Spotted Calla and Yellow Calla. Ryohitsu Shibuya. The author, 1430 Grant Rd., Mountain View, Calif., 1956. 62 pp.

Electronic Computers, Principles and Applications. T. E. Ivall. Iliffe, London; Philosophical Library, New York, 1956. 167 pp. $10.

Straight to the Heart. A personal account of thoughts and feelings while undergoing heart surgery. George Lawton. International Universities Press, New York, 1956. 347 pp. $5.

Mind and the World-Order. Clarence I. Lewis. Dover, New York, 1956 (unabridged republication of ed. 1). 446 pp. Paper, $1.95.

Miscellaneous Publications

(Inquiries concerning these publications should be addressed, not to Science, *but to the publisher or agency sponsoring the publication.)*

Systematics of the Suborder Tubulifera (Thysanoptera) in California. Publ. in Entomology, vol. 13. H. Edwin Cott. University of California Press, Berkeley, 1956. 216 pp. $3.50.

Mammals of the Anglo-Egyptian Sudan. No. 3377. Proc. of the U.S. National Museum, vol. 106. Henry W. Setzer. Smithsonian Institution, Washington, 1956. 141 pp.

Rabbits. A subject bibliography. Special Bibliography No. 3. Laura I. Makepeace. Bibliographical Center for Research, Denver Public Library, Denver, Colo. 1956. 81 pp. $2.

Resources for the Future, Annual Report. For the year ending 30 Sept. 1956. Resources for the Future, 1145 19 St., NW, Washington, 1956. 85 pp.

Meetings and Societies

Psychobiological Development of the Child

In 1953 the World Health Organization created a study group to "discuss the influences of biological, psychological, and cultural factors in development." The interdisciplinary and international group included, among others, J. Bowlby (London), E. Erikson (Stockbridge), G. R. Hargreaves (Leeds), B. Inhelder (Geneva), E. E. Krapf (Geneva), K. Lorenz (Seewiesen), M. Mead (New York), K. A. Melin (Stockholm), M. Monnier (Geneva), J. Piaget (Sorbonne), A. Rémond (Paris), J. M. Tanner (London), W. Grey Walter (London), R. Zazzo (Paris).

The scope of the conference was to review the field from its various aspects, such as somatic growth, electroencephalography, child psychology, theory of instinct, psychoanalysis, and cultural anthropology, with an attempt to coordinate the results obtained in these various branches of science. Under the able chairmanship of F. Fremont-Smith (Macy Foundation), the meetings developed in the form of idea conferences, formal presentations being limited, and emphasis placed on free discussion.

Piaget summarized the principal problems arising from the material presented in the first three sessions in a number of questions, of which the following may be mentioned. *Factors of development*: Besides the traditional three main factors in development, hereditary, environmental, and social, a fourth factor, successive "equilibrium stages," should be envisaged. *Search for a common language*: In view of the difficulties of interdisciplinary communication and understanding, the question whether conceptual models translatable from one realm to another can be found becomes imperative. *Stages of development versus continuous development*: Is development a continuous process, or does it take place in a series of steps or stages, and how far is either concept applicable to development as a whole and to individual developmental processes? *Cognitive and affective aspects of development*: How far can the development of cognitive functions (as studied by Piaget and his school) be correlated with the developmental stages indicated by psychoanalysis?

The fourth meeting, held in Geneva 20–26 Sept. 1956, was devoted to a discussion of these and related questions. Among other presentations, Inhelder, Piaget, and Noelting showed a film (*Cognitive Development of the Child*) which vividly illustrates the highlights of the research done by Piaget and coworkers (development of notions of space, of conservation, of reasoning). Bowlby presented material related to mother-child separation. Erikson reviewed social aspects of psychoanalysis. Monnier compared the development of the electroencephalographic pattern in the child with Piaget's stages of the development of cognitive functions. Bertalanffy presented general system theory as a possible means of a "common language" and discussed symbolism as a characteristic unique to man and not sufficiently taken into account by conventional psychoanalytic theory.

The fourth conference was planned to be the final one, but in view of many remaining problems and new viewpoints brought into discussion, a continuation of the study group is envisaged. The proceedings of the meetings are published under the title *Discussion on Child Development* (J. M. Tanner and B. Inhelder, editors) by Tavistock Publications, Ltd., London, of which the first and second volumes have appeared, and the consecutive volumes are to follow soon.

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Meeting Notes

■ The first Pan American Cancer Cytology Congress will be held in Miami Beach, Fla., 25–29 Apr. The State Department has invited the Ministries of Health of the 21 nations of the Western Hemisphere to send representatives to the meeting.

Recent advances in basic cancer research will be surveyed by experts from countries of North and South America. Special emphasis will be placed upon gynecological cancer and the revolutionary role of cervical cytology as a screening test for uterine cancer, which was recently perfected for population screening. The role of cytodiagnosis in improving surgical treatment in lung, prostatic, and gastrointestinal cancer will be discussed. Of special interest to practitioners of medicine will be explanations of procedural details and methodology for the application of cytodiagnosis for early detection of cancer in the physician's office.

Those who wish to present papers at the Congress should apply to the program chairman, Dr. Wayne Rogers, P.O. Box 633, Coral Gables, Fla. Address inquiries about scientific exhibits or moving picture presentations to the chairman, Dr. Homer L. Pearson, P.O. Box 633, Coral Gables, Fla.

■ An Electronic Components Symposium will be held at the Morrison Hotel in Chicago 1–3 May. The meeting is sponsored annually by the American Institute of Radio Engineers, the Radio-Electronics-Television manufacturers Association, and the West Coast Electronic Manufacturers Association, with the active participation of agencies of the Department of Defense and the National Bureau of Standards.

Papers will be given in eight areas: high-temperature components, radiation effects, component reliability, passive components, active components, instrumentation and measurements, materials development, and general component needs. Further information can be obtained by writing to J. S. Powers, Electronic Components Symposium, 84 E. Randolph St., Chicago 1, Ill.

■ Stanford University School of Medicine will present a Postgraduate Conference in Surgery from 18 Mar. through 22 Mar. 1957. Registration is unlimited and will be open to holders of the M.D. degree.

Patients with common surgical problems will be presented. The surgical anatomy of the region under consideration will be demonstrated while the patient is taken to surgery. After the anatomical demonstration the operation will be broadcast in black and white television. Programs and further information may be obtained from the Office of the Dean, Stanford University School of Medicine, 2398 Sacramento St., San Francisco 15, Calif.

■ The annual Institute of Radio Engineers National Convention and Radio Engineering Show will be held at the Waldorf-Astoria Hotel and the New York Coliseum 18–21 Mar. A program of 55 technical sessions is being set up

by the Technical Program Committee with the assistance of all the IRE professional groups. Two highlight sessions, "Future use of air space" and "Microminiaturization—the ultimate technique," will be held the evening of 19 Mar. All four floors of the Coliseum will be set aside for the use of 840 exhibitors at the Radio Engineering Show.

■ The nation's first comprehensive demonstration of systems presently in use for the organization, storage, and retrieval of recorded information, together with a symposium on information-handling problems and techniques, will be presented at Western Reserve University in Cleveland, Ohio, 15–17 Apr. The activities will be sponsored by the School of Library Science of Western Reserve University in conjunction with its Center for Documentation and Communication Research, and by the Council on Documentation Research, a group recently formed by representatives of organizations in government, industry, and education to promote cooperation among those concerned with information.

Further information may be obtained from Dean Jesse H. Shera, School of Library Science, Western Reserve University, Cleveland 6, Ohio.

■ A Symposium on Nondestructive Tests that have been developed in the Field of Nuclear Energy will be held at the Morrison Hotel in Chicago, Ill., 16–18 Apr. The symposium is being sponsored jointly by the American Institute of Chemical Engineers, the American Nuclear Society, the American Society for Testing Materials, and the Society for Nondestructive Testing.

The results of 15 years of research and development in testing applications in the nuclear field will be presented to persons who are interested in the industrial applications of nondestructive test methods. The recently declassified papers presented will be divided into three categories: (i) reactor materials, including fuel, sheath or cladding, control, and moderator material; (ii) complete fuel assemblies; and (iii) miscellaneous.

Papers will be presented in the morning and afternoon sessions each day, and in the evenings of the first and second days there will be panel discussions in which the authors on the day's program will take part. The chairman of the symposium is W. J. McGonnagle, Argonne National Laboratory.

■ A symposium on the formation and stabilization of free radicals will be held at the National Bureau of Standards 18–20 Sept. The meeting will be sponsored jointly by the Applied Physics Laboratory of Johns Hopkins University, Catholic University of America, and the National Bureau of Standards.

Recent advances in low-temperature physics, high-polymer research, and other fields have stimulated interest in the isolation and study of free radicals. A number of industrial, Government, and university laboratories are now conducting research programs on free radicals. The programs should yield results of broad significance in basic chemistry and physics. The September conference is expected to provide a valuable medium for exchange of information in this rapidly growing field. Further information on the program may be obtained from Dr. A. M. Bass, Free Radicals Research Section, National Bureau of Standards, Washington 25, D.C.

Society Elections

■ AAAS Alaska Division: pres., Victor P. Hessler, University of Alaska; v. pres., Frank Pauls, Territorial Department of Health; sec., Clyde J. Beers, U.S. Coast and Geodetic Survey, College, Alaska; treas., John Buckley, University of Alaska. Representative to the AAAS Council is C. T. Elvey.

■ American Public Health Association: pres., John W. Knutson, Assistant Surgeon General, U.S. Public Health Service; pres.-elect, Roy J. Morton, Oak Ridge National Laboratory; treas., Charles Glen King, Nutrition Foundation Inc.; exec.-sec., Reginald M. Atwater, APHA, 1790 Broadway, New York, N.Y.

■ Oklahoma Academy of Science: pres., D. E. Howell, Oklahoma Agricultural and Mechanical College; v. pres., George Goodman, University of Oklahoma; sec.-treas., Philip Smith, Oklahoma University School of Medicine; permanent sec., J. Teague Self, University of Oklahoma.

■ Academy Conference: pres., Thelma C. Heatwole, Staunton, Va.; pres.-elect, John Yarborough, Meredith College, Raleigh, N.C.; sec., John G. Arnold, Loyola University, New Orleans, La.

Forthcoming Events

February

10–12. **Canadian Ceramic Soc., 55th annual, Niagara Falls, Ont., Canada. (L. C. Keith, 49 Turner Road, Toronto, Ont.)**

14. **Present Status of Heart Sound Production and Recording, symp., Buffalo, N.Y. (R. M. Kohn, Univ. of Buffalo, 2183 Main Street, Buffalo 14, N.Y.)**

14. **Significance of Nucleic Acid Derivatives in Nutrition, Assoc. of Vitamin Chemists, Chicago, Ill. (M. Freed, Dawe's Laboratories, Inc., 4800 S. Richmond St., Chicago 32.)**

14–15. **Transistor Circuits, conf., Philadelphia, Pa. (G. H. Royer, Westinghouse Electric Corp., 356 Collins Ave., Pittsburgh 6, Pa.)**

15–16. **National Soc. of Professional Engineers, Charleston, S.C. (P. H. Robbins, 2029 K St., NW, Washington 6.)**

15–17. **National Assoc. for Research in Science Teaching, annual, Atlantic City, N.J. (C. M. Pruitt, Univ. of Tampa, Tampa, Fla.)**

16. **Management of Acute Myocardial Infarction, symp., American College of Cardiology, New York, N.Y. (P. Reichert, Secy., ACC, Empire State Bldg., New York.)**

18–20. **American Educational Research Assoc., annual, Atlantic City, N. J. (F. W. Hubbard, AERA, 1201 16 St., NW, Washington 6.)**

18–22. **American Soc. of Civil Engineers, Jackson, Miss. (W. H. Wisely, ASCE, 33 W. 39 St., New York 18.)**

18–22. **Endocrinology: Hormones in Blood, Ciba Found. Colloq. (by invitation), London, England. (G. E. W. Wolstenholme, 41 Portland Place, London.)**

21–23. **National Soc. of College Teachers of Education, annual, Chicago, Ill. (C. A. Eggertsen, School of Education, Univ. of Michigan, Ann Arbor.)**

23. **American Mathematical Soc., New Haven, Conn. (J. H. Curtiss, AMS, 190 Hope St., Providence 6, R.I.)**

23. **Oregon Acad. of Science, annual, Monmouth, (F. A. Gilfillan, Oregon State College, Corvallis.)**

24–28. **American Inst. of Mining, Metallurgical and Petroleum Engineers, annual, New Orleans, La. (E. O. Kirkendall, AIME, 29 W. 39 St., New York 18.)**

24–28. **International College of Surgeons, 10th biennial cong., Mexico, D.F., Mexico. (M. Thorek, ICS, 850 W. Irving Park Rd., Chicago 13, Ill.)**

25–28. **American Soc. of Heating and Air-Conditioning Engineers, Chicago, Ill. (A. V. Hutchinson, ASHAE, 62 Worth St., New York 13.)**

26–28. **Western Joint Computer Conf., Los Angeles, Calif. (M. J. Mendelson, Norden-Ketay Corp., 13210 Crenshaw Blvd., Gardena, Calif.)**

March

1–2. **American Physical Soc., Norman, Okla. (K. K. Darrow, Columbia Univ., New York 27.)**

1–3. **National Wildlife Federation, annual, Washington, D.C. (C. H. Callison, 232 Carroll St., NW, Washington 12.)**

3–6. **American Inst. of Chemical Engineers, White Sulphur Springs, W.Va. (F. J. Van Antwerpen, AIChE, 25 W. 45 St., New York 36.)**

3–9. **American Soc. of Photogrammetry, 23rd annual, joint with American Cong. on Surveying and Mapping, 17th annual, Washington, D.C. (C. E. Palmer, ASP, 1515 Massachusetts Ave., NW, Washington 5.)**

4. **Wildlife Soc., annual, Washington, D.C. (D. L. Leedy, Fish and Wildlife Service, Dept. of the Interior, Washington 25.)**

4–6. **National Biophysics Conf., Columbus, Ohio. (H. P. Schwan, School of Medicine, Univ. of Pennsylvania, Philadelphia 4.)**

4–8. Analytical Chemistry and Applied Spectroscopy, Pittsburgh, Pa. (L. M. Melnick, U.S. Steel Corp., Applied Research Lab., Monroeville, Pa.)

7–9. American Orthopsychiatric Assoc., 34th annual, Chicago, Ill. (M. F. Langer, AOA, 1790 Broadway, New York 19.)

7–9. Fundamental Cancer Research, 11th annual symp., Houston, Tex. (L. Dmochowski, M. D. Anderson Hospital, Texas Medical Center, Houston 25.)

7–9. Optical Soc. of America, semiannual, New York, N.Y. (S. S. Ballard, Scripps Inst. of Oceanography, San Diego 52, Calif.)

10–16. Nuclear Engineering and Science Cong., 2nd, Philadelphia, Pa. (Engineers Joint Council, 29 W. 39 St., New York 18.)

11–15. National Assoc. of Corrosion Engineers, 13th annual, St. Louis, Mo. (R. T. Effinger, Shell Oil Co., Deer Park Refinery, Houston, Tex.)

13–15. Society of Exploration Geophysicists, 10th annual midwestern, Fort Worth, Tex. (G. A. Grimm, Tide Water Associated Oil Co., Box 2131, Midland, Tex.)

14. Effect of Radiation on Foods, Assoc. of Vitamin Chemists, Chicago, Ill. (M. Freed, Dawe's Laboratories, Inc., 4800 S. Richmond St., Chicago 32.)

15. Fats in Human Nutrition, AMA symp., New Orleans, La. (Council on Foods and Nutrition, American Medical Assoc., 535 N. Dearborn, Chicago 10, Ill.)

18–21. Institute of Radio Engineers, natl. convention, New York, N.Y. (B. Warriner, IRE, 1 E. 79 St., New York 21.)

19–21. American Meteorological Soc., 151st national, Chicago, Ill. (K. C. Spengler, AMS, 3 Joy St., Boston 8, Mass.)

20–22. National Health Forum, Cincinnati, Ohio. (National Health Council, 1790 Broadway, New York 19.)

20–23. National Science Teachers Assoc., annual, Cleveland, Ohio. (R. H Carleton, NSTA, 1201 16 St., NW, Washington 6.)

21–23. American Physical Soc., Philadelphia, Pa. (K. K. Darrow, APS, Columbia Univ., New York 27, N.Y.)

21–23. International Assoc. for Dental Research, annual, Atlantic City, N.J. (D. Y. Burrill, 129 E. Broadway, Louisville 2, Ky.)

21–23. Michigan Acad. of Science, Arts and Letters, annual, Detroit, Mich. (R. F. Haugh, Dept. of English, Univ. of Michigan, Ann Arbor.)

22–23. Heart: Law-Medicine Problem, Cleveland, Ohio. (O. Schroeder, Jr., Law-Medicine Center, Western Reserve Univ., Cleveland 6.)

23–28. American Soc. of Tool Engineers, 25th annual, Houston, Tex. (R. Gebers, 10700 Puritan, Detroit 38, Mich.)

24–27. American Assoc. of Dental Schools, annual, Atlantic City, N.J. (M. W. McCrea, 42 S. Greene St., Baltimore 1, Md.)

25–28. American Acad. of General Practice, 9th annual scientific assembly, St. Louis, Mo. (M. F. Cahal, AAGP, Volker Blvd. at Brookside, Kansas City 12, Mo.)

25–29. Western Metal Exposition and Congress, 10th, Los Angeles, Calif. (W. H. Eisenman, 7301 Euclid Ave., Cleveland 3, Ohio.)

26–28. Mechanisms for the Development of Drug Resistance in Microorganisms, Ciba Foundation Symp. (by invitation), London, England. (G. E. W. Wolstenholme, 41 Portland Pl., London, W.1.)

26–28. Weather Radar Conf., 6th, sponsored by American Meteorological Soc., Cambridge, Mass. (K. C. Spengler, 3 Joy St., Boston 8, Mass.)

27–29. American Power Conf., 19th annual, Chicago, Ill. (R. A. Budenholzer, Illinois Inst. of Technology, 35 W. 33 St., Chicago 16.)

27–29. National Committee on Alcoholism, annual, Chicago, Ill. (Miss E. Jensen, NCA, 2 E. 103 St., New York 29.)

31–9. Pan American Cong. of Social Work, 3rd, San Juan, P.R. (Mrs. M. Velez de Perez, Apartado 3271, San Juan.)

April

1–4. American Assoc. of Petroleum Geologists, 42nd annual, St. Louis, Mo. (R. H. Dott, AAPG, Box 979, Tulsa, Okla.)

1–4. International Anesthesia Research Soc., cong., Phoenix, Ariz. (A. W. Friend, Wade Park Manor, Cleveland 6, Ohio.)

1–5. Assoc. of American Geographers, annual, Cincinnati, Ohio (B. W. Adkinson, Reference Dept., Library of Congress, Washington 25.)

5–6. American Mathematical Soc., New York, N.Y. (J. H. Curtiss, AMS, 190 Hope St., Providence 6, R.I.)

7–10. Pan American Assoc. of Ophthalmology, 4th interim cong., New York, N.Y. (B. F. Payne, 17 E. 72 St., New York 21.)

7–12. American Chemical Soc., Miami, Fla. (A. H. Emery, ACS, 1155 16 St., NW, Washington 6.)

8. Phi Lambda Upsilon, Miami, Fla. (T. B. Cameron, Dept. of Chemistry, Univ. of Cincinnati, Cincinnati 21, Ohio.)

8–10. American Soc. of Mechanical Engineers, spring, Birmingham, Ala. (C. E. Davies, ASME, 29 W. 39 St., New York 18.)

8–12. Food Bacteriology, internatl. symp., Cambridge, England. (Dr. Mossel, Central Inst. for Nutrition Research T.N.O., Catharijnesingel 61, Utrecht, Netherlands.)

8–12. Surface Activity, 2nd world cong., London, England. (Congress Secy., 14 Belgrave Sq., London, S.W. 1.)

9–10. Industrial Electronics Education Conf., annual, Chicago, Ill. (E. A. Roberts, Armour Research Foundation, Illinois Inst. of Technology, Chicago 16.)

10–12. Nuclear Instrumentation Conf.,

natl., Atlanta, Ga. (H. Kindler, Instrument Soc. of America, 313 Sixth Ave., Pittsburgh, Pa.)

10–13. Conference on Embryology and Experimental Morphology, Cambridge, England. (D. R. Newth, Dept. of Zoology, University College London, Gower St., London W.C. 1.)

11–13. Southwestern Inst. of Radio Engineers Conf. and Electronics Show, 9th annual, with 2nd National Simulation Conf., Houston, Tex. (F. C. Smith, Jr., Box 13058, Houston 19.)

12–13. Colorado–Wyoming Acad. of Science, annual, Fort Collins, Colo. (O. W. Olsen, Colorado A.&M. College, Fort Collins.)

12–13. Eastern Psychological Assoc., annual, New York, N.Y. (G. G. Lane, Dept. of Psychology, Univ. of Delaware, Newark.)

12–13. New Orleans Acad. of Sciences, New Orleans, La. (A. Welden, Dept. of Biology, Newcomb College, New Orleans.)

12–14. American Assoc. for Cancer Research, Chicago, Ill. (H. J. Creech, Inst. for Cancer Research, Fox Chase, Philadelphia 11, Pa.)

12–14. American Assoc. of Physical Anthropologists, annual, Ann Arbor, Mich. (J. H. Spuhler, Dept. of Human Genetics, Univ. of Michigan Medical School, Ann Arbor.)

12–14. National Speleological Soc., Natural Bridge, Va. (Mrs. M. McKenzie, 1407 Hickory Ct., Broyhill Park, Falls Church, Va.)

13. South Carolina Academy of Science, annual, Columbia (Miss M. Hess, Box 114, Winthrop College, Rock Hill, S.C.)

14–20. American Physiological Soc., Chicago, Ill. (M. O. Lee, APS, 9650 Wisconsin Ave., NW, Washington 14.)

15–17. Systems for Information Retrieval, symp., Cleveland, Ohio. (J. H. Shera, School of Library Science, Western Reserve Univ., Cleveland 6.)

15–18. American Personnel and Guidance Assoc. and constituent divisions: American College Personnel Assoc., American School Counselor Assoc., National Assoc. of Guidance Supervisors and Counselor Trainers, National Vocational Guidance Assoc., Student Personnel Assoc. for Teacher Education; Detroit, Mich. (A. A. Hitchcock, APGA, 1534 O St., NW, Washington 5.)

15–18. Host-Specificity and Parallel Evolution among Parasitic Insects and Worms, symp., Neuchatel, Switzerland. (J. G. Baer, C.P. 2, Neuchatel 7.)

15–19. American Assoc. of Immunologists, annual, Chicago, Ill. (F. S. Cheever, Graduate School of Public Health, Univ. of Pittsburgh, Pittsburgh 13, Pa.)

15–19. American Soc. for Experimental Pathology, annual, Chicago, Ill. (C. C. Erickson, Inst. of Pathology, Univ. of Tennessee, 858 Madison Ave., Memphis.)

15–19. American Soc. for Pharmacology and Experimental Therapeutics, Chicago, Ill. (H. Hodge, Dept. of Pharmacology, Univ. of Rochester, Rochester, N.Y.)

15–19. Federation of American Societies for Experimental Biology, annual, Chicago, Ill. (M. O. Lee, FASEB, 9650 Wisconsin Ave., Washington 14.)

15–19. High Energy Nuclear Physics Conf., 7th annual, Rochester, N.Y. (R., Marshak, Univ. of Rochester, Rochester.)

15–20. American Inst. of Nutrition, annual, Chicago, Ill. (R. W. Engel, Dept. of Biochemistry and Nutrition, Virginia Polytechnic Inst., Blacksburg 13, Va.)

16–18. Nuclear Tests for Nondestructive Testing Applications, symp., Chicago, Ill. (American Soc. for Testing Materials, 1916 Race St., Philadelphia 3, Pa.)

17–19. American Assoc. of Anatomists, annual, Baltimore, Md. (L. B. Flexner, School of Medicine, Univ. of Pennsylvania, Philadelphia 4.)

18–20. Assoc. of Southeastern Biologists, annual, Athens, Ga. (J. C. Dickinson, Jr., Univ. of Florida, Gainesville.)

18–20. Ohio Acad. of Science, annual, Bowling Green. (R. W. Dexter, Dept. of Biology, Kent State Univ., Kent, Ohio.)

18–20. Southern Soc. for Philosophy and Psychology, annual, Gatlinburg, Tenn. (W. B. Webb, U.S. Navy School of Aviation Medicine, Pensacola, Fla.)

18–20. Venereal Disease Postgrad. Conf., 26th, Memphis, Tenn. (H. Packer, Dept. of Preventive Medicine, Univ. of Tennessee College of Medicine, Memphis 3.)

19–20. Arkansas Acad. of Science, annual, Fayetteville. (L. F. Bailey, University of Arkansas, Fayetteville.)

19–20. Seismological Soc. of America, annual, Los Angeles, Calif. (P. Byerly, Bacon Hall, Univ. of California, Berkeley 4.)

23–25. Chemistry and Biology of Mucopolysaccharides, Ciba Foundation Symp. (by invitation only), London, England. (G. E. W. Wolstenholme, 41 Portland Pl., London, W.1.)

23–25. Solid State Devices in Electric Circuits, symp., New York, N.Y. (J. Griesmann, Microwave Research Inst., 55 Johnson St., Brooklyn 1, N.Y.)

23–26. American Industrial Hygiene Assoc., annual, St. Louis, Mo. (G. D. Clayton, AIHA, 14125 Prevost, Detroit 27, Mich.)

24–26. Purity Control by Thermal Analysis, IUPAC, Amsterdam, Netherlands. (W. M. Smit, Central Inst. for Physico-Chemical Constants, Biltstraat 172, Utrecht, Netherlands.)

25–27. American Physical Soc., Washington, D.C. (K. K. Darrow, APS, Columbia Univ., New York 27.)

25–29. Pan American Cancer Cytology Cong., Miami, Fla. (J. E. Ayre, New York Univ., New York, N.Y.)

26–27. American Assoc. of University Professors, annual, New York, N.Y. (R. F. Fuchs, AAUP, 1785 Massachusetts Ave., NW, Washington 6.)

26–27. Iowa Acad. of Science, annual, Cedar Falls. (J. L. Laffoon, Dept. of Zoology and Entomology, Iowa State College, Ames.)

26–27. Kentucky Acad. of Science, Mammoth Cave. (G. Levey, Berea College, Berea, Ky.)

EQUIPMENT NEWS

All inquiries concerning items listed here should be addressed to Science, *Room 604, 11 W. 42 St., New York 36, N.Y. Include the name(s) of the manufacturer(s) and the department number(s).*

■ MASS SPECTROMETER that operates on a radio-frequency principle rather than on a magnetic principle is designed for continuous-process stream analysis and control and for laboratory analysis. The new gas analyzer alternately monitors any six preselected gases in the range between mass 12 and mass 100. An accessory permits cyclic monitoring of selected gases at the rate of one every 10 sec. (Beckman Instruments, Inc., Dept. S125)

■ PARTICLE RESOLVER utilizes flying-spot scanning to convert a two-dimensional distribution of density into a varying voltage/time relationship, which in turn is used to produce an 8- by 8-in. picture of a microscopic subject on a picture tube. Magnification is variable from 200 to 8000 diameters; resolution is 0.1 μ. The instrument, which is made by Cinema-Television, Ltd., of London, can also be used to count automatically the number of particules within the field of the objective. Minimum particle size is 0.6 μ. A sizing unit permits selection of a lower limit to the size of particles to be counted; this limit is from 0.6 to 160 μ in 60 increments. (Marconi Instruments, Ltd., Dept. S126)

■ RECORDING OSCILLOGRAPH that will accept up to 24 individual signals simultaneously and record them on a strip chart is of the direct ink-writing type but utilizes a light-beam type of galvanometer. (Century Electronics and Instruments, Inc., Dept. S127)

■ FLAME SPECTROMETER provides simultaneous analysis of sodium, potassium, calcium, and magnesium in biological samples. The instrument consists of a collapsed-beam version of a Wadsworth 750-mm, concave-grating spectrometer and associated electronic circuits. It requires a 1-ml sample. Exit slits are located on the peaks of the lines giving the greatest sensitivity for Na, K, Ca, and Mg. Additional slits observe the background on one or both sides of the lines. The photomultiplier output for the background is electronically subtracted from the output for the line plus background. Concentration ranges are as follows: Na, 0.01 to 30 ppm; Ca, 0.1 to 100 ppm; K and Mg, 1.0 to 1000 ppm. The precision is approximately ±3% at 1 ppm for Na and Ca and at 10 ppm for K and Mg. (Jarrell Ash Co., Dept. S124)

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The University of Alberta invites applications for the position of assistant professor of pharmacology, effective not later than 1 September 1957, at a salary of $5000–$6200 per annum, with annual increments of $300. Duties include undergraduate and graduate teaching and a program of research. Applicants possessing a medical degree, in addition to qualifications in pharmacology, will be given preference.

Applications for the above position should include a recent photograph or snapshot, a curriculum vitae, and the name of three references, and should be sent to the **Dean of Medicine, University of Alberta, Edmonton, Alberta, Canada.** X

Chemist, M.S. or equivalent in organic (medicinal) chemistry with experience or training in botany to assist in evaluation of scientific data concerning natural products. Eastern pharmaceutical manufacturer offers liberal benefits. Send complete résumé. Box 4, SCIENCE. 1/18

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POSITIONS OPEN

POSITIONS REQUIRING DEGREES IN MEDICINE OR SCIENCE: (a) **Assistant Toxicologist;** Ph.D. thoroughly trained experienced in pharmacology and/or biochemistry, might consider B.S. or M.S. outstandingly experienced; assist noted toxicologist, supervise staff personnel, New England laboratory, noted eastern concern; $8000–$10,000. (b) **Bacteriologist;** advanced degree preferred, must have hospital experience; to head section, 400-bed general hospital, expansion program under way; to $5000; Midwest. (c) **Biochemist;** excellent opportunity for qualified M.S. or Ph.D., head department, newly expanded and superbly equipped laboratory, 300-bed general hospital; reorganize and develop department, full responsibility all specialized procedures; to $7500; Chicago area. Woodward Medical Personnel Bureau, 185 North Wabash, Chicago. X

Research Scientist to collaborate in urological applications of ultrasound. Capacity for thoughtful independent investigation with broad mechanical aptitudes at Columbia Medical School. Available now. Box 10, SCIENCE. 1/18

(a) Scientists, Ph.D. degrees, biochemistry or chemistry, experienced pharmaceutical field; opportunities for section or projects leaders and research scientists at bench level; new research laboratories, long-established organization; $7000–$9000; Midwest. **(b) Bacteriologist** qualified to head department, 450-bed teaching hospital; medical center; East. **(c) Associate Medical Director;** preferably physician well trained in surgery, medicine, or pediatrics; pharmaceutical company; Pacific Coast. **(d) Clinical Chemist,** Ph.D.; large general hospital, East; $7000–$10,000. **(e) Endocrinologist;** new laboratory, famed research institution; Midwest. **(f) Advertising Writer** to direct program, ethical drug company; East. S1-3 Medical Bureau, Burneice Larson, Director, 900 North Michigan, Chicago. X

Teaching and Research Assistantships available, providing partial or complete support during graduate program. Gross anatomy course to be offered this summer is open to graduate students and undergraduate students past junior year, and will provide basic training for teaching to those otherwise unprepared. Inquire Dr. Paul G. Roofe, Chairman, Department of Anatomy, University of Kansas, Lawrence. 1/18, 25

Teaching and Research Positions, Ph.D., at large midwestern Catholic university in vertebrate zoology, invertebrate zoology, embryology, and physiology. Academic rank and salary commensurate with qualifications. New chairman to be selected. All applications held in strict confidence. Box 6, SCIENCE. 1/18, 25; 2/1, 8

POSITIONS WANTED

Biochemist–Food Scientist, Ph.D. Established academic and research reputation; fluent writer and speaker. Seeks challenging leadership opportunity, academic, institutional, or industrial. Box 11, SCIENCE. 1/18, 25

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Biochemist, Ph.D., male; background in physiology and analytical chemistry; 2 years' teaching experience. Desires teaching post with research opportunity. Box 18, SCIENCE. X

Clinical Research. Medical-sales education and professional service director, 3 years; college instructor, medical technology and physical sciences, 3 years; A.B., psychology; B.S., biology; 3 years' medicine with medical writing experience; desires clinical research or related position in pharmaceutical industry. Box 26, SCIENCE. X

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Medical Director; 5 years' experience pharmaceuticals, antibiotics at large eastern company; certified internist, knowledge of basic sciences; completing postgraduate course. Box 25, SCIENCE. 1/25; 2/1, 8, 15, 22

Microbiologist, Ph.D., 30; 2 years as chief bacteriologist in consulting laboratory directing vitamins, antibiotics, germicides, and food bacteriology. Desires academic or industrial position in eastern area. Box 27, SCIENCE. X

POSITIONS WANTED

Microbiologist, Ph.D., major parasitology; some postdoctoral teaching and research experience. Desires teaching position, preferably with research opportunities. Box 15, SCIENCE. X

Microbiologist, Ph.D. Experienced, interested in biochemical analysis, cytochemistry, photomicroscopy, infectious diseases, and metabolism. Publications. Box 23, SCIENCE. X

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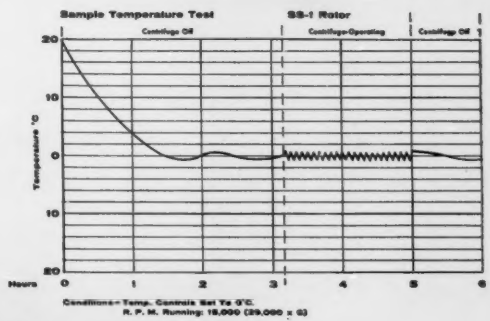

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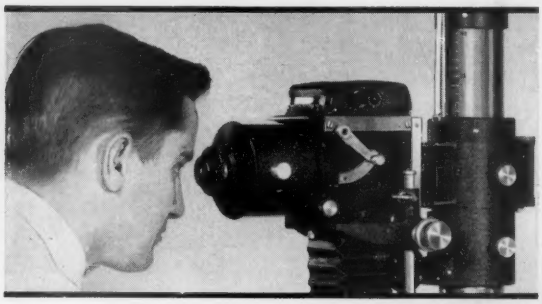

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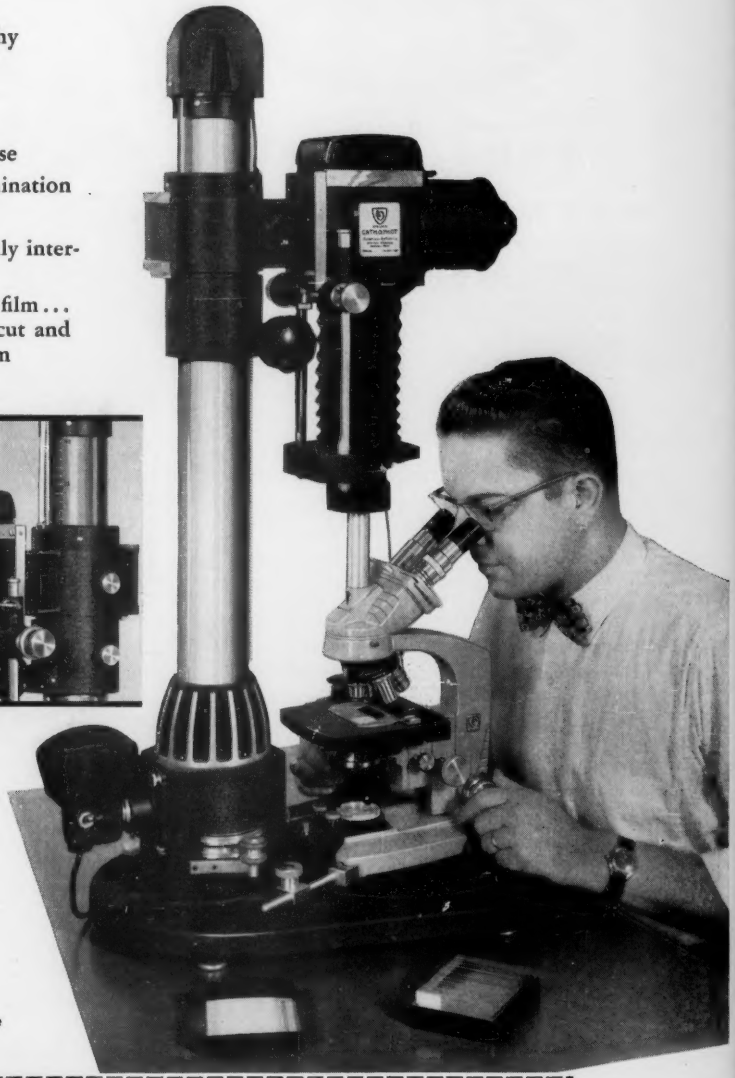

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